U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

SEARCH REQUEST FORM

Requestor's Name: ERIC ANGELL

Serial Number: 09/766,442

Date: 2/27/03

Phone: 703-605-1165

Art Unit: 1635 12th Floor DISC 11E12 mailbox

Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevent citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevent claim(s).

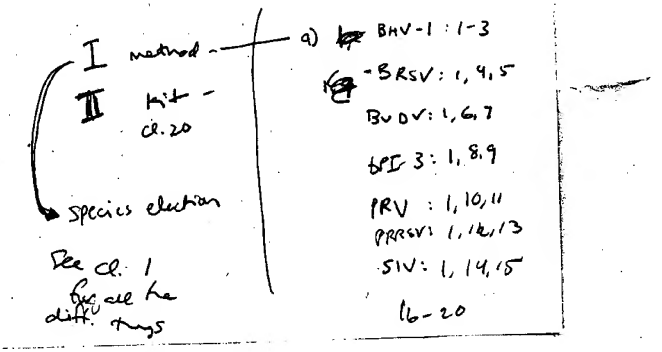
Search compound of claim 1 (attached)

if necessary use the following terms to limit result set:

vaccine (or related terms)

RSV (respiratory syncitial virus)

Bovine RSV



STAFF USE ONLY

Date completed: 2-27-03

Searcher: [illegible]

Terminal time: 23

Elapsed time: [illegible] 30

CPU time: _____

Total time: _____

Number of Searches: _____

Number of Databases: _____

Search Site

_____ STIC

_____ CM-1

_____ Pre-S

Type of Search

_____ N.A. Sequence

_____ A.A. Sequence

1 Structure

_____ Bibliographic

Vendors

_____ IG

369 STN

_____ Dialog

_____ APS

_____ Geninfo

_____ SDC

_____ DARC/Questel

_____ Other

PTO-1590 (8-90)

```
=> fil reg; d stat que l7
FILE 'REGISTRY' ENTERED AT 15:20:13 ON 27 FEB 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   26 FEB 2003  HIGHEST RN 495373-62-1
DICTIONARY FILE UPDATES:  26 FEB 2003  HIGHEST RN 495373-62-1

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf


L5                STR

                10
                Ak
                |
                |       11
                O 9     Me
                |       |
                |       |6
Ak— O— CH2- CH- CH2- N— Ak— G3
1   2   3   4   5   |   7   8
                    |
                    Me
                    12


VAR G3=OH/NH2
NODE ATTRIBUTES:
CONNECT IS E1  RC AT   1
CONNECT IS E2  RC AT   7
CONNECT IS E1  RC AT  10
DEFAULT MLEVEL IS ATOM
GGCAT   IS HIC  AT   1 > alkyls at nodes 1 & 10 have >6 carbons
GGCAT   IS HIC  AT  10
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS M2-X3 C  AT   7 - alkyl at node 7 has 3-3 carbons

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  12

STEREO ATTRIBUTES: NONE
L7            41 SEA FILE=REGISTRY SSS FUL L5

100.0% PROCESSED  32156 ITERATIONS                41 ANSWERS
SEARCH TIME: 00.00.01


=> fil capl; d que nos 120; d que nos 122
```

FILE 'CAPLUS' ENTERED AT 15:20:14 ON 27 FEB 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 27 Feb 2003 VOL 138 ISS 9
FILE LAST UPDATED: 26 Feb 2003 (20030226/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
L5              STR
L7           41 SEA FILE=REGISTRY SSS FUL L5
L10         168 SEA FILE=CAPLUS ABB=ON  L7
L15       31763 SEA FILE=CAPLUS ABB=ON  VACCINES/CT
L16        7884 SEA FILE=CAPLUS ABB=ON  IMMUNOTHERAPY/CW OR THERAPEUTICS/CT(L)I
                MMUNO
L17        5596 SEA FILE=CAPLUS ABB=ON  IMMUNIZATION/CT
L18          63 SEA FILE=CAPLUS ABB=ON  VACCINATION/CT
L19       12338 SEA FILE=CAPLUS ABB=ON  IMMUNOSTIMULA?/CT
L20          27 SEA FILE=CAPLUS ABB=ON  L10 AND (L15 OR L16 OR L17 OR L18 OR
                L19)


L5              STR
L7           41 SEA FILE=REGISTRY SSS FUL L5
L10         168 SEA FILE=CAPLUS ABB=ON  L7
L21         118 SEA FILE=CAPLUS ABB=ON  BRSV? OR RESPIRATORY SYNCITIAL
L22           0 SEA FILE=CAPLUS ABB=ON  L21 AND L10
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=> fil uspatf; d que nos 126;d que nos 128; s 126 or 128

FILE 'USPATFULL' ENTERED AT 15:20:14 ON 27 FEB 2003

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 27 Feb 2003 (20030227/PD)
FILE LAST UPDATED: 27 Feb 2003 (20030227/ED)
HIGHEST GRANTED PATENT NUMBER: US6526583
HIGHEST APPLICATION PUBLICATION NUMBER: US2003041363
CA INDEXING IS CURRENT THROUGH 27 Feb 2003 (20030227/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 27 Feb 2003 (20030227/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2002
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2002

>>> USPAT2 is now available. USPATFULL contains full text of the <<<
>>> original, i.e., the earliest published granted patents or <<<
>>> applications. USPAT2 contains full text of the latest US <<<
>>> publications, starting in 2001, for the inventions covered in <<<

>>> USPATFULL. A USPATFULL record contains not only the original <<<
>>> published document but also a list of any subsequent <<<
>>> publications. The publication number, patent kind code, and <<<
>>> publication date for all the US publications for an invention <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc. <<<

>>> USPATFULL and USPAT2 can be accessed and searched together <<<
>>> through the new cluster USPATALL. Type FILE USPATALL to <<<
>>> enter this cluster. <<<
>>> <<<
>>> Use USPATALL when searching terms such as patent assignees, <<<
>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
L5              STR
L7           41 SEA FILE=REGISTRY SSS FUL L5
L23          39 SEA FILE=USPATFULL ABB=ON  L7
L24        6387 SEA FILE=USPATFULL ABB=ON  VACCINES/CT OR IMMUNIZATION/CT OR
                VACCINATION/CT OR IMMUNOSTIMULAT?/CT
L25         991 SEA FILE=USPATFULL ABB=ON  IMMUNOTHERAPY/IT OR (THERAPEUTICS(L)
                IMMUNO)/IT
L26           4 SEA FILE=USPATFULL ABB=ON  L23 AND (L24 OR L25)
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L5              STR
L7           41 SEA FILE=REGISTRY SSS FUL L5
L23          39 SEA FILE=USPATFULL ABB=ON  L7
L27         244 SEA FILE=USPATFULL ABB=ON  BRSV? OR RESPIRATORY SYNCITIAL
L28           2 SEA FILE=USPATFULL ABB=ON  L23 AND L27
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L53           5 L26 OR L28
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=> fil medl; d que nos 132; d que nos 136

FILE 'MEDLINE' ENTERED AT 15:20:15 ON 27 FEB 2003

FILE LAST UPDATED: 26 FEB 2003 (20030226/UP). FILE COVERS 1958 TO DATE.

On June 9, 2002, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2003 vocabulary. See http://www.nlm.nih.gov/mesh/summ2003.html for a description on changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
L5              STR
L7           41 SEA FILE=REGISTRY SSS FUL L5
L29          39 SEA FILE=MEDLINE ABB=ON  L7
L30       83276 SEA FILE=MEDLINE ABB=ON  IMMUNIZATION+NT/CT
L31       85966 SEA FILE=MEDLINE ABB=ON  VACCINES+NT/CT
L32           2 SEA FILE=MEDLINE ABB=ON  L29 AND (L30 OR L31)
```

```
L5              STR
L7           41 SEA FILE=REGISTRY SSS FUL L5
L29          39 SEA FILE=MEDLINE ABB=ON  L7
L33         274 SEA FILE=MEDLINE ABB=ON  BRSV? OR RESPIRATORY SYNCITIAL
L34         179 SEA FILE=MEDLINE ABB=ON  RESPIRATORY SYNCYTIAL VIRUS, BOVINE/CT

L35        1632 SEA FILE=MEDLINE ABB=ON  RESPIRATORY SYNCYTIAL VIRUS INFECTIONS
                +NT/CT
L36           0 SEA FILE=MEDLINE ABB=ON  L29 AND (L33 OR L34 OR L35)
```

```
=> fil toxcenter; d que nos l52

FILE 'TOXCENTER' ENTERED AT 15:20:16 ON 27 FEB 2003
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FILE COVERS 1907 TO 25 Feb 2003 (20030225/ED)

This file contains CAS Registry Numbers for easy and accurate substance
identification.

TOXCENTER has been enhanced with new files segments and search fields.
See HELP CONTENT for more information.

TOXCENTER thesauri in the /CN, /CT, and /MN fields incorporate the
MeSH 2003 vocabulary.  See http://www.nlm.nih.gov/mesh/summ2003.html
for a description on changes.


L5              STR
L7           41 SEA FILE=REGISTRY SSS FUL L5
L47          77 SEA FILE=TOXCENTER ABB=ON  L7
L48       68341 SEA FILE=TOXCENTER ABB=ON  VACCINE# OR VACCINAT? OR IMMUNIZ?
                OR IMMUNIS?
L49       18708 SEA FILE=TOXCENTER ABB=ON  IMMUNOTHERAP?
L50        5060 SEA FILE=TOXCENTER ABB=ON  IMMUNOSTIMULA?
L51          50 SEA FILE=TOXCENTER ABB=ON  BRSV? OR RESPIRATORY SYNCITIAL
L52          19 SEA FILE=TOXCENTER ABB=ON  L47 AND (L48 OR L49 OR L50 OR L51)
```

```
=> fil agricola; d que nos l37

FILE 'AGRICOLA' ENTERED AT 15:20:16 ON 27 FEB 2003


FILE COVERS 1970 TO 19 Feb 2003 (20030219/ED)

Compiled and distributed by the National Agricultural Library
of the Department of Agriculture of the United States of
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reserved.  (2002)

This file contains CAS Registry Numbers for easy and accurate
substance identification.


L5              STR
L7           41 SEA FILE=REGISTRY SSS FUL L5
L37           0 SEA FILE=AGRICOLA ABB=ON  L7
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```
=> fil caba; d que nos 138

FILE 'CABA' ENTERED AT 15:20:17 ON 27 FEB 2003
COPYRIGHT (C) 2003 CAB INTERNATIONAL (CABI)

FILE COVERS 1973 TO 14 Feb 2003 (20030214/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.


L5              STR
L7           41 SEA FILE=REGISTRY SSS FUL L5
L38           0 SEA FILE=CABA ABB=ON  L7


=> fil biosis; d que nos 144

FILE 'BIOSIS' ENTERED AT 15:20:18 ON 27 FEB 2003
COPYRIGHT (C) 2003 BIOLOGICAL ABSTRACTS INC.(R)

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 26 February 2003 (20030226/ED)


L5              STR
L7           41 SEA FILE=REGISTRY SSS FUL L5
L39          10 SEA FILE=BIOSIS ABB=ON  L7
L40      140600 SEA FILE=BIOSIS ABB=ON  VACCINE# OR VACCINAT? OR IMMUNIZ? OR
                IMMUNIS?
L41       26730 SEA FILE=BIOSIS ABB=ON  IMMUNOTHERAP?
L42       10664 SEA FILE=BIOSIS ABB=ON  IMMUNOSTIMULA?
L43         270 SEA FILE=BIOSIS ABB=ON  BRSV? OR RESPIRATORY SYNCITIAL
L44           0 SEA FILE=BIOSIS ABB=ON  L39 AND (L40 OR L41 OR L42 OR L43)


=> fil biotechno; d que nos 146

FILE 'BIOTECHNO' ENTERED AT 15:20:18 ON 27 FEB 2003
COPYRIGHT (C) 2003 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE LAST UPDATED: 18 FEB 2003       <20030218/UP>
FILE COVERS 1980 TO DATE.

>>>  SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN
     /CT AND BASIC INDEX  <<<


L5              STR
L7           41 SEA FILE=REGISTRY SSS FUL L5
L46           0 SEA FILE=BIOTECHNO ABB=ON  L7


=> dup rem 120,153,132,152
FILE 'CAPLUS' ENTERED AT 15:20:38 ON 27 FEB 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE 'USPATFULL' ENTERED AT 15:20:38 ON 27 FEB 2003

FILE 'MEDLINE' ENTERED AT 15:20:38 ON 27 FEB 2003

FILE 'TOXCENTER' ENTERED AT 15:20:38 ON 27 FEB 2003

PROCESSING COMPLETED FOR L20
PROCESSING COMPLETED FOR L53
PROCESSING COMPLETED FOR L32
PROCESSING COMPLETED FOR L52
L54 37 DUP REM L20 L53 L32 L52 (16 DUPLICATES REMOVED)
ANSWERS '1-27' FROM FILE CAPLUS
ANSWERS '28-32' FROM FILE USPATFULL
ANSWER '33' FROM FILE MEDLINE
ANSWERS '34-37' FROM FILE TOXCENTER

=> d ibib abs hitstr 1-32; d iall 33-37

L54 ANSWER 1 OF 37 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 1
ACCESSION NUMBER: 2002:10302 CAPLUS
DOCUMENT NUMBER: 136:74555
TITLE: Vaccine against foot-and-mouth disease
INVENTOR(S): King, Andrew; Burman, Alison; Audonnet, Jean-Christophe; Lombard, Michel
PATENT ASSIGNEE(S): Merial, Fr.
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000251	A1	20020103	WO 2001-FR2042	20010627
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2810888	A1	20020104	FR 2000-8437	20000629
AU 2001070678	A5	20020108	AU 2001-70678	20010627

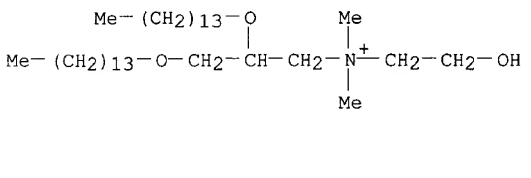
PRIORITY APPLN. INFO.: FR 2000-8437 A 20000629
WO 2001-FR2042 W 20010627

OTHER SOURCE(S): MARPAT 136:74555

AB The invention concerns a vaccine against foot-and-mouth disease, using as antigen an efficient amt. of empty capsids of the foot-and-mouth virus, said empty capsids being obtained by expressing, in eukaryotic cells, cDNA of the P1 region of the foot-and-mouth virus genome coding for the capsid and cDNA of the region of the foot-and-mouth virus genome coding for protease 3C, the vaccine further comprising a carrier or excipient pharmaceutically acceptable in veterinary medicine. The invention also concerns the insertion of a mutation in the sequence VP2 (introducing a cysteine), thereby stabilizing the empty capsids and the resulting viruses.

IT **153312-64-2**, Dmrie

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vaccine against foot-and-mouth disease)
RN 153312-64-2 CAPLUS
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 2 OF 37 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 2
ACCESSION NUMBER: 2001:167832 CAPLUS
DOCUMENT NUMBER: 134:212748
TITLE: Lipid-nucleic acid compositions for stimulating cytokine secretion and inducing an immune response
INVENTOR(S): Semple, Sean C.; Harasym, Troy O.; Klimuk, Sandra K.; Kojic, Ljiljiana D.; Bramson, Jonathan L.; Mui, Barbara; Hope, Michael J.
PATENT ASSIGNEE(S): Inex Pharmaceuticals Corp., Can.
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001015726	A2	20010308	WO 2000-CA1013	20000828
WO 2001015726	A3	20010726		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000068139	A5	20010326	AU 2000-68139	20000828
BR 2000013834	A	20020423	BR 2000-13834	20000828
EP 1212085	A2	20020612	EP 2000-956004	20000828
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: US 2000-176406P P 20000113
US 1999-151211P P 19990826
WO 2000-CA1013 W 20000828

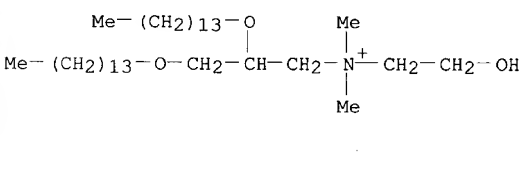
AB Lipid-nucleic acid particles can provide therapeutic benefits, even when the nucleic acid is not complementary to coding sequences in target cells. It has been found that lipid-nucleic acid particles, including those contg. non-sequence specific oligodeoxynucleotides, can be used to stimulate cytokine secretion, thus enhancing the overall immune response

of a treated mammal. Further, immune response to specific target antigens can be induced by administration of an antigenic mol. in assocn. with lipid particles contg. non-sequence specific oligodeoxynucleotides. The nucleic acid which is included in the lipid-nucleic acid particle can be a phosphodiester (i.e., an oligodeoxynucleotide consisting of nucleotide residues joined by phosphodiester linkages) or a modified nucleic acid which includes phosphorothioate or other modified linkages, and may suitably be one which is non-complementary to the human genome, such that it acts to provide immunostimulation in a manner which is independent of conventional base-pairing interactions between the nucleic acid and nucleic acids of the treated mammal. In particular, the nucleic acid may suitably contain an immune-stimulating motif such as a CpG motif, or an immune stimulating palindromic sequence. The cationic lipid included in the nucleic acid particles may be suitably selected from among DODAP, DODMA, DMDMA, DOTAP, DC-Chol, DDAB, DODAC, DMRIE, DOSPA and DOGS. In addn., the lipid particle may suitably contain a modified aggregation-limiting lipid such as a PEG-lipid, a PAO-lipid or a ganglioside.

IT **153312-64-2**, DMRIE
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lipid-nucleic acid compns. for stimulating cytokine secretion and inducing an immune response)

RN 153312-64-2 CAPLUS

CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



● Br^-

L54 ANSWER 3 OF 37 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 3
ACCESSION NUMBER: 2001:101291 CAPLUS
DOCUMENT NUMBER: 134:161880
TITLE: cDNAs encoding the Flt-3 receptor ligand and there use as adjuvants in vector vaccines
INVENTOR(S): Hermanson, Gary George
PATENT ASSIGNEE(S): Vical Inc., USA
SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001009303	A2	20010208	WO 2000-US20679	20000731
WO 2001009303	A3	20010816		

W: CA, JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

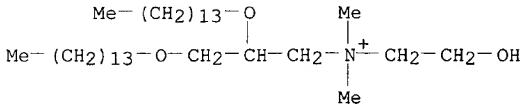
PRIORITY APPLN. INFO.: US 1999-146170P P 19990730

AB A method of increasing the strength of the immune response of vector

vaccines using an expression vector for the Flt3 ligand is described. The vaccines are made of independent non-integrating expression vectors: one encodes the antigen or a cytokine and the other encodes the Flt3 ligand. The present invention also provides a method broadly directed to improving immune response of a vertebrate in need of immunotherapy by administering in vivo, into a tissue of a vertebrate, a Flt-3 ligand-encoding polynucleotide and one or more antigen- or cytokine-encoding polynucleotides. The polynucleotides are incorporated into the cells of the vertebrate in vivo, and a prophylactically or therapeutically effective amt. of a Flt-3 ligand and one or more antigens is produced in vivo.

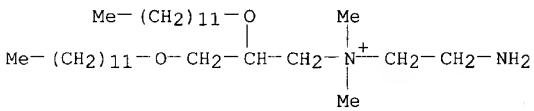
IT **153312-64-2**, DMRIE **208040-06-6**, GAP-DLRIE
299207-54-8, GAP-DMORIE
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in delivery of vector vaccines; cDNAs encoding Flt-3 receptor ligand and there use as adjuvants in vector vaccines)

RN 153312-64-2 CAPLUS
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



● Br^-

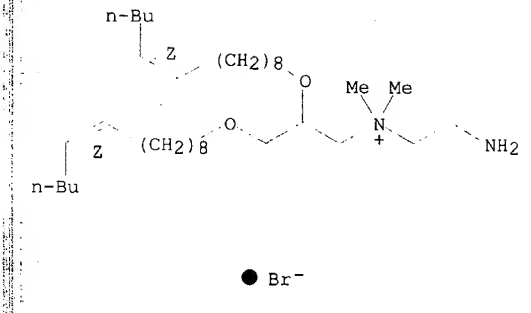
RN 208040-06-6 CAPLUS
CN 1-Propanaminium, N-(2-aminoethyl)-2,3-bis(dodecyloxy)-N,N-dimethyl-, bromide (9CI) (CA INDEX NAME)



● Br^-

RN 299207-54-8 CAPLUS
CN 1-Propanaminium, N-(2-aminoethyl)-N,N-dimethyl-2,3-bis[(9Z)-9-tetradecenyloxy]-, bromide (9CI) (CA INDEX NAME)

Double bond geometry as shown.

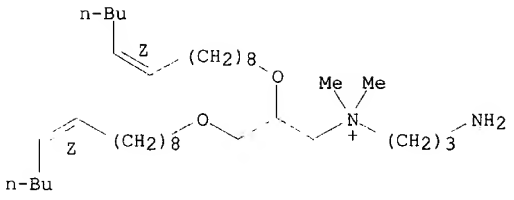


L54 ANSWER 4 OF 37 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 4
ACCESSION NUMBER: 2001:409275 CAPLUS
DOCUMENT NUMBER: 136:198465
TITLE: Vaxfectin enhances antigen specific antibody titers and maintains Th1 type immune responses to plasmid DNA immunization
AUTHOR(S): Reyes, L.; Hartikka, J.; Bozoukova, V.; Sukhu, L.; Nishioka, W.; Singh, G.; Ferrari, M.; Enas, J.; Wheeler, C. J.; Manthorpe, M.; Wloch, M. K.
CORPORATE SOURCE: Department of Cell Biology, Vical Incorporated, San Diego, CA, 92121, USA
SOURCE: Vaccine (2001), 19(27), 3778-3786
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Antigen specific immune responses were characterized after i.m. immunization of BALB/c mice with 5 antigen encoding plasmid DNAs (pDNAs) complexed with Vaxfectin, a cationic lipid formulation. Vaxfectin increased IgG titers for all of the antigens with no effect on the CTL responses to the 2 antigens for which CTL assays were performed. Both antigen specific IgG1 and IgG2a were increased, although IgG2a remained greater than IgG1. Furthermore, Vaxfectin had no effect on IFN-.gamma. or IL-4 prodn. by splenocytes re-stimulated with antigen, suggesting that the Th1 type responses typical of i.m. pDNA immunization were not altered. Studies with IL-6 -/- mice suggest that the antibody enhancement is IL-6 dependent and results in a correlative increase in antigen specific antibody secreting cells.
IT **370108-99-9**, Vaxfectin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Vaxfectin enhanced antigen-specific antibody titers maintaining Th1 type immune responses to plasmid DNA vaccines)
RN 370108-99-9 CAPLUS
CN 1-Propanaminium, N-(3-aminopropyl)-N,N-dimethyl-2,3-bis[(9Z)-9-tetradecenyloxy]-, bromide, mixt. with (1R)-1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl bis(3,7,11,15-tetramethylhexadecanoate) (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 370108-98-8
CMF C36 H73 N2 O2 . Br

Double bond geometry as shown.



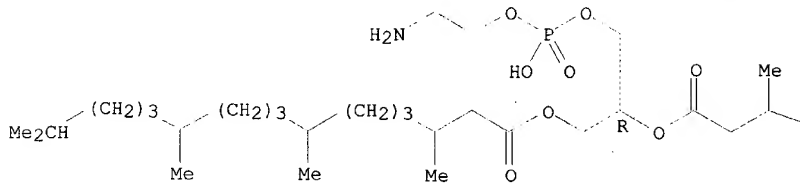
● Br^-

CM 2

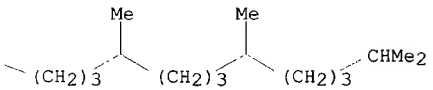
CRN 201036-16-0
CMF C45 H90 N O8 P

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 5 OF 37 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 5
ACCESSION NUMBER: 2001:146642 CAPLUS
DOCUMENT NUMBER: 135:330213
TITLE: Vaxfectin enhances the humoral immune response to plasmid DNA-encoded antigens
AUTHOR(S): Hartikka, J.; Bozoukova, V.; Ferrari, M.; Sukhu, L.; Enas, J.; Sawdey, M.; Wloch, M. K.; Tonsky, K.; Norman, J.; Manthorpe, M.; Wheeler, C. J.
CORPORATE SOURCE: Department of Cell Biology, Vical Incorporated, San Diego, CA, 92121, USA
SOURCE: Vaccine (2001), 19(15-16), 1911-1923
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal

Searched by Barb O'Bryen, STIC 308-4291

LANGUAGE: English

AB This report characterizes Vaxfectin, a novel cationic and neutral lipid formulation which enhances antibody responses when complexed with an antigen-encoding plasmid DNA (pDNA). In mice, i.m. injection of Vaxfectin formulated with pDNA encoding influenza nucleoprotein (NP) increased antibody titers .ltoreq. 20-fold, to levels that could not be reached with pDNA alone. As little as 1 .mu.g of pDNA formulated with Vaxfectin per muscle resulted in higher anti-NP titers than that obtained with 25 .mu.g naked pDNA. The antibody titers in animals injected with Vaxfectin-pDNA remained higher than in the naked pDNA controls for at least 9 mo. The enhancement in antibody titers was dependent on the Vaxfectin dose and was accomplished without diminishing the strong anti-NP cytolytic T cell response typical of pDNA-based vaccines. In rabbits, complexing pDNA with Vaxfectin enhanced antibody titers .ltoreq. 50-fold with needle and syringe injections and also augmented humoral responses when combined with a needle-free injection device. Vaxfectin did not facilitate transfection and/or increase synthesis of .beta.-galactosidase reporter protein in muscle tissue. ELISPOT assays performed on bone marrow cells from vaccinated mice showed that Vaxfectin produced a 3- to 5-fold increase in the no. of NP-specific plasma cells. Thus, Vaxfectin should be a useful adjuvant for enhancing pDNA-based vaccinations.

IT **370108-99-9P**, Vaxfectin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Vaxfectin enhances the humoral immune response to plasmid DNA-encoded antigens)

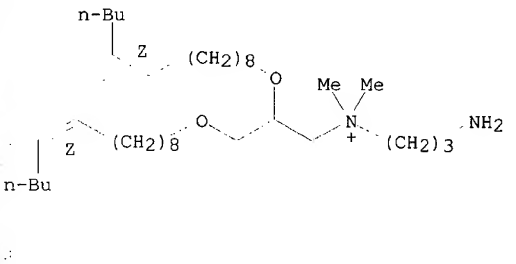
RN 370108-99-9 CAPLUS

CN 1-Propanaminium, N-(3-aminopropyl)-N,N-dimethyl-2,3-bis[(9Z)-9-tetradecenyloxy]-, bromide, mixt. with (1R)-1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl bis(3,7,11,15-tetramethylhexadecanoate) (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 370108-98-8
CMF C36 H73 N2 O2 . Br

Double bond geometry as shown.

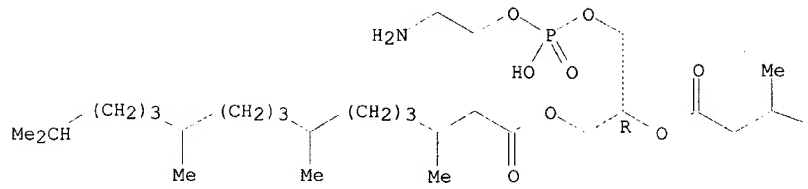


CM 2

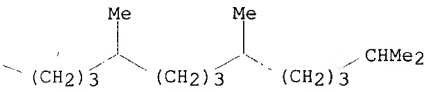
CRN 201036-16-0
CMF C45 H90 N O8 P

Absolute stereochemistry.

PAGE 1-A

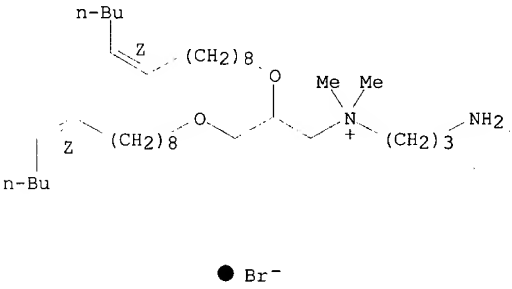


PAGE 1-B



IT **370108-98-8P**, VC 1052
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Vaxfectin enhances the humoral immune response to plasmid DNA-encoded antigens)
RN 370108-98-8 CAPLUS
CN 1-Propanaminium, N-(3-aminopropyl)-N,N-dimethyl-2,3-bis[(9Z)-9-tetradecenyloxy]-, bromide (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 6 OF 37 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 6
ACCESSION NUMBER: 2001:490587 CAPLUS
DOCUMENT NUMBER: 135:362424
TITLE: Highly efficient gene delivery by mRNA electroporation in human hematopoietic cells: superiority to lipofection and passive pulsing of mRNA and to electroporation of plasmid cDNA for tumor antigen loading of dendritic cells
AUTHOR(S): Van Tendeloo, Viggo F. I.; Ponsaerts, Peter; Lardon, Filip; Nijs, Griet; Lenjou, Marc; Van Broeckhoven, Christine; Van Bockstaele, Dirk R.; Berneman, Zwi N.

Searched by Barb O'Bryen, STIC 308-4291

CORPORATE SOURCE: Laboratory of Experimental Hematology, Antwerp University Hospital, University of Antwerp, Antwerp, Belg.
SOURCE: Blood (2001), 98(1), 49-56
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Designing effective strategies to load human dendritic cells (DCs) with tumor antigens is a challenging approach for DC-based tumor vaccines. Here, a cytoplasmic expression system based on mRNA electroporation to efficiently introduce tumor antigens into DCs is described. Preliminary expts. in K562 cells using an enhanced green fluorescent protein (EGFP) reporter gene revealed that mRNA electroporation as compared with plasmid DNA electroporation showed a markedly improved transfection efficiency (89% vs. 40% EGFP+ cells, resp.) and induced a strikingly lower cell toxicity (15% death rate with mRNA vs. 51% with plasmid DNA). Next, mRNA elec. troporation was applied for nonviral transfection of different types of human DCs, including monocyte-derived DCs (Mo-DCs), CD34+ progenitor-derived DCs (34-DCs) and Langerhans cells (34-LCs). High-level transgene expression by mRNA electroporation was obtained in more than 50% of all DC types. MRNA-electroporated DCs retained their phenotype and maturational potential. Importantly, DCs electroporated with mRNA-encoding Melan-A strongly activated a Melan-A-specific cytotoxic T lymphocyte (CTL) clone in an HLA-restricted manner and were superior to mRNA-lipofected or -pulsed DCs. Optimal stimulation of the CTL occurred when Mo-DCs underwent maturation following mRNA transfection. Strikingly, a nonspecific stimulation of CTL was obsd. when DCs were transfected with plasmid DNA. The data clearly demonstrate that Mo-DCs electroporated with mRNA efficiently present functional antigenic peptides to cytotoxic T cells. Therefore, electroporation of mRNA-encoding tumor antigens is a powerful technique to charge human dendritic cells with tumor antigens and could serve applications in future DC-based tumor vaccines.

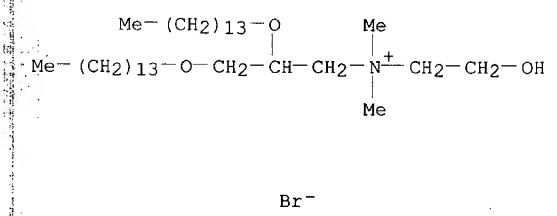
IT **189203-05-2**, DMRIE-C
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipofection with; highly efficient gene delivery by mRNA electroporation in human hematopoietic cells for tumor antigen loading of dendritic cells)

RN 189203-05-2 CAPLUS

CN Cholest-5-en-3-ol (3.beta.)-, mixt. with N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-1-propanaminium bromide (9CI) (CA INDEX NAME)

CM 1

CRN 153312-64-2
CMF C35 H74 N O3 . Br

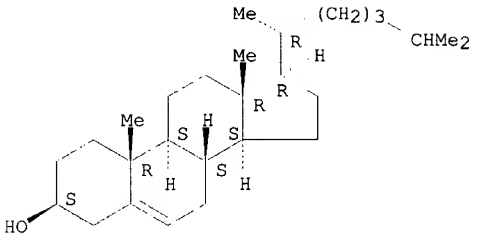


CM 2

CRN 57-88-5

CMF C27 H46 O

Absolute stereochemistry.



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 7 OF 37 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 7
ACCESSION NUMBER: 2000:707018 CAPLUS
DOCUMENT NUMBER: 133:280556
TITLE: Adjuvant compositions and methods for enhancing immune responses to polynucleotide-based vaccines
INVENTOR(S): Wheeler, Carl J.
PATENT ASSIGNEE(S): Vical Incorporated, USA
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000057917	A2	20001005	WO 2000-US8282	20000324
WO 2000057917	A3	20010104		
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1165140	A2	20020102	EP 2000-919777	20000324
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002540173	T2	20021126	JP 2000-607666	20000324

PRIORITY APPLN. INFO.: US 1999-126340P P 19990326
WO 2000-US8282 W 20000324

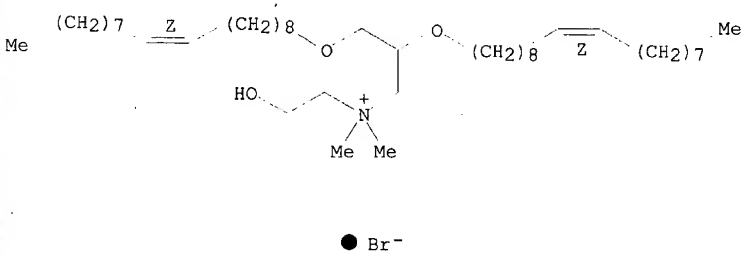
AB The invention provides adjuvants, immunogenic compns., and methods useful for polynucleotide-based vaccination and immune response. In particular, the invention provides an adjuvant of cytofectin:co-lipid mixt. wherein cytofectin is GAP-DMORIE.

IT **153312-60-8**, DORIE **153312-64-2**, DMRIE
154486-25-6, GAP-DMRIE **188949-12-4**, DMORIE
199171-54-5, DLRIE **208040-06-6**, GAP-DLRIE
299207-53-7, DDRIE **299207-54-8**, GAP-DMORIE
299207-55-9, GAP-DPRIE
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(adjuvant compns. contg. cytofectin:co-lipid mixts. and methods for enhancing immune responses to polynucleotide-based vaccines)

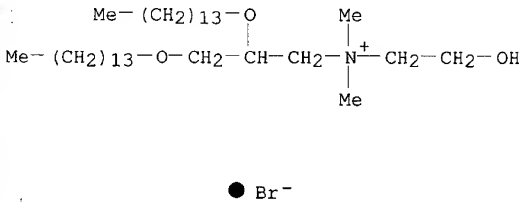
RN 153312-60-8 CAPLUS
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis[(9Z)-9-

octadecenyloxy]-, bromide (9CI) (CA INDEX NAME)

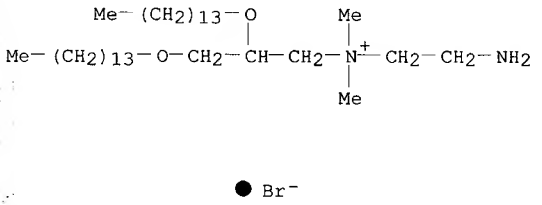
Double bond geometry as shown.



RN 153312-64-2 CAPLUS
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)

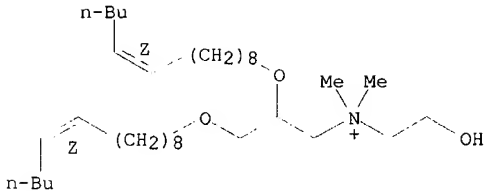


RN 154486-25-6 CAPLUS
CN 1-Propanaminium, N-(2-aminoethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



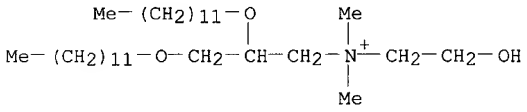
RN 188949-12-4 CAPLUS
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis[(9Z)-9-tetradecenyloxy]-, bromide (9CI) (CA INDEX NAME)

Double bond geometry as shown.



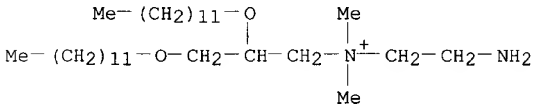
● Br^-

RN 199171-54-5 CAPLUS
CN 1-Propanaminium, 2,3-bis(dodecyloxy)-N-(2-hydroxyethyl)-N,N-dimethyl-, bromide (9CI) (CA INDEX NAME)



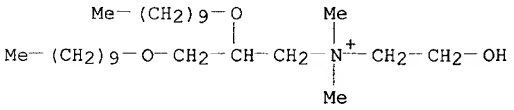
● Br^-

RN 208040-06-6 CAPLUS
CN 1-Propanaminium, N-(2-aminoethyl)-2,3-bis(dodecyloxy)-N,N-dimethyl-, bromide (9CI) (CA INDEX NAME)



● Br^-

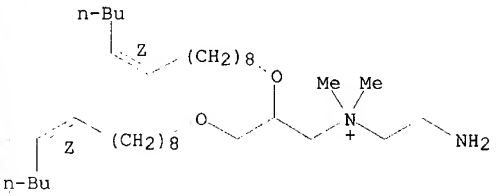
RN 299207-53-7 CAPLUS
CN 1-Propanaminium, 2,3-bis(decyloxy)-N-(2-hydroxyethyl)-N,N-dimethyl-, bromide (9CI) (CA INDEX NAME)



Br^-

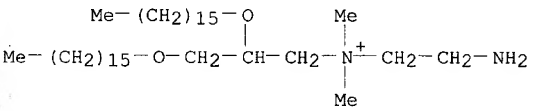
RN 299207-54-8 CAPLUS
CN 1-Propanaminium, N-(2-aminoethyl)-N,N-dimethyl-2,3-bis[(9Z)-9-tetradecenyloxy]-, bromide (9CI) (CA INDEX NAME)

Double bond geometry as shown.



● Br^-

RN 299207-55-9 CAPLUS
CN 1-Propanaminium, N-(2-aminoethyl)-2,3-bis(hexadecyloxy)-N,N-dimethyl-, bromide (9CI) (CA INDEX NAME)



● Br^-

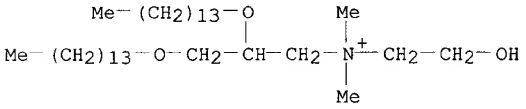
L54 ANSWER 8 OF 37 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 8
ACCESSION NUMBER: 2000:573482 CAPLUS
DOCUMENT NUMBER: 134:146025
TITLE: Effectiveness of combined interleukin 2 and B7.1 vaccination strategy is dependent on the sequence and order: A liposome-mediated gene therapy treatment for bladder cancer
AUTHOR(S): Larchian, William A.; Horiguchi, Yutaka; Nair, Smita K.; Fair, William R.; Heston, Warren D. W.; Gilboa, Eli
CORPORATE SOURCE: Department of Urology, The Cleveland Clinic Foundation, Cleveland, OH, 44195, USA
SOURCE: Clinical Cancer Research (2000), 6(7), 2913-2920
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors have developed a novel liposome-mediated immunogene therapy using interleukin 2 (IL-2) and B7.1 in a murine bladder cancer model. A carcinogen-induced murine bladder cancer cell line, MBT-2, was transfected with cationic liposome 1,2-dimyristyloxypropyl-3-dimethyl-hydroxyethyl ammonium bromide/dioleolylphosphatidylethanolamine and IL-2 plasmid. The optimized transfection condition generated IL-2 levels of 245-305 ng/106 cells/24 h, 100-fold higher than the levels seen with retrovirus

transfection. Ninety percent of the peak level of IL-2 prodn. was maintained for up to 11 days after transfection. Animal studies were conducted in C3H/HeJ female mice with 2.times.104 MBT-2 cells implanted orthotopically on day 0. Multiple vaccination schedules were performed with i.p. injection of 5.times.106 IL-2 and/or B7.1 gene-modified cell prepns. The greatest impact on survival was obsd. with the day 5, 10, and 15 regimen. Control animals receiving retrovirally gene-modified MBT-2/IL-2 cell prepns. had a median survival of 29 days. Animals receiving the IL-2 liposomally gene-modified cell prepn. alone had a median survival of 46 days. Seventy-five percent of animals receiving IL-2 followed by B7.1 gene-modified tumor vaccines were the only group to show complete tumor-free survival at day 60. All of these surviving animals rejected the parental MBT-2 tumor rechallenge and survived at day 120 with a high CTL response. Thus, liposome-mediated transfection demonstrates a clear advantage as compared with the retroviral system in the MBT-2 model. Multi-agent as opposed to single-agent cytokine gene-modified tumor vaccines were beneficial. These "targeted" sequential vaccinations using IL-2 followed by B7.1 gene-modified tumor cells increased a systemic immune response that translated into increased survival.

IT **153312-64-2**, DMRIE
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposome contg.; combined interleukin 2 and B7.1 vaccination strategy in liposome-mediated gene therapy of bladder cancer is dependent on sequence and order)

RN 153312-64-2 CAPLUS

CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



● Br^-

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 9

ACCESSION NUMBER: 1998:750931 CAPLUS
DOCUMENT NUMBER: 130:109034
TITLE: Immunotherapy of established tumors in mice by intratumoral injection of interleukin-2 plasmid DNA: induction of CD8+ T-cell immunity
AUTHOR(S): Saffran, Douglas C.; Horton, Holly M.; Yankauckas, Michelle A.; Anderson, Deborah; Barnhart, Kerry M.; Abai, Anna M.; Hobart, Peter; Manthorpe, Marston; Norman, Jon A.; Parker, Suezanne E.
CORPORATE SOURCE: Vical Inc., San Diego, CA, 92121, USA
SOURCE: Cancer Gene Therapy (1998), 5(5), 321-330
CODEN: CGTHEG; ISSN: 0929-1903
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Intratumoral (i.t.) injection of a plasmid DNA vector encoding the murine interleukin-2 (IL-2) gene was used to treat established renal cell carcinoma (Renca) tumors in BALB/c mice. Tumor regression was obsd. in

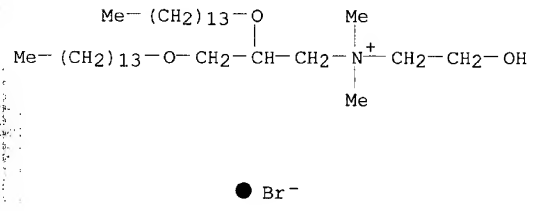
60-90% of mice that were injected i.t. for 4 days with IL-2 plasmid DNA complexed with the cationic lipid DMRIE/DOPE ((.+-.)-N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-1-propanaminium bromide/dioleoylphosphatidylethanolamine). The mice remained tumor-free until the conclusion of the study, which was 4 mo after tumor challenge. In a rechallenge expt., mice that were rendered tumor-free for 6 mo by IL-2 plasmid DNA treatment rejected a subsequent challenge of Renca cells but could not reject a challenge with the unrelated, syngeneic CT-26 tumor. Spleen cells from cured mice contained Renca-specific cytotoxic T lymphocytes, and adoptive transfer of mixed lymphocyte cultures into naive mice at 2 days after challenge with Renca cells prevented tumor growth. In vivo depletion of T-cell subsets at the time of i.t. injection with IL-2 plasmid DNA demonstrated that CD8+ T cells, but not CD4+ T cells, were the primary effectors of the antitumor response.

IT **213186-72-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunotherapy of established tumors in mice by intratumoral injection of interleukin-2 plasmid DNA induces CD8+ T-cell immunity)

RN 213186-72-2 CAPLUS
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide, mixt. with 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl di-(9Z)-9-octadecenoate (9CI) (CA INDEX NAME)

CM 1

CRN 153312-64-2
CMF C35 H74 N O3 . Br

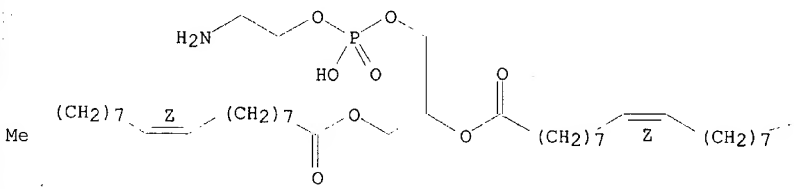


CM 2

CRN 2462-63-7
CMF C41 H78 N O8 P

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

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REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 10 OF 37 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 10
ACCESSION NUMBER: 1998:750929 CAPLUS
DOCUMENT NUMBER: 130:108901
TITLE: Lipofection indirectly increases expression of endogenous major histocompatibility complex class I molecules on tumor cells
AUTHOR(S): Fox, Bernard A.; Drury, Marcie; Hu, Hong-Ming; Cao, Zhuwei; Huntzicker, Erik G.; Qie, Wenxia; Urba, Walter J.
CORPORATE SOURCE: Laboratory of Molecular and Tumor Immunology, Robert W. Franz Cancer Research Center, Providence Portland Medical Center, Earle A. Chiles Research Institute, Portland, OR, 97213, USA
SOURCE: Cancer Gene Therapy (1998), 5(5), 307-312
CODEN: CGTHEG; ISSN: 0929-1903
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English

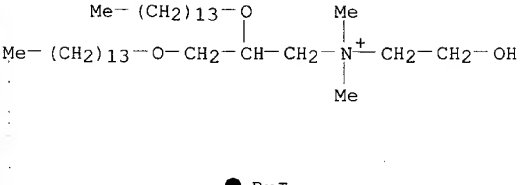
AB Direct intratumoral injection of a lipid/DNA complex encoding an allogeneic major histocompatibility complex (MHC) class I mol. leads to regression of both an immunogenic murine tumor and also melanoma lesions in some patients. We have sought to understand the mechanism(s) for this augmentation of antitumor activity. While optimizing parameters for in vitro gene transfer into the D5 subclone of B16BL6, it was noted that lipofected tumors not only expressed the new alloantigen but also exhibited increased expression of endogenous MHC class I, both H-2 Kb and H-2 Db. This increase in expression was not restricted to the small percentage of cells that expressed the transfected gene, but appeared to affect the majority of cells in culture. Class I expression was not increased by lipopolysaccharide, DNA alone, lipid, or lipid/lipopolysaccharide mixts. Enhanced class I expression required a DNA/lipid complex and was greatest when parameters optimized for gene transfer of the alloantigen were used. All DNA plasmids tested had this effect, including one plasmid whose DNA was not transcribed because it lacked an expression cassette. Because of the crit. role that MHC class I antigens play in immune recognition, we propose that lipid complex-mediated gene transfer may provide immunol. advantages beyond those that are attributable to expression of the specific gene transferred.

IT **213186-72-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipofection indirectly increases expression of endogenous MHC class I mols. on tumor cells and enhances antitumor activity)

RN 213186-72-2 CAPLUS
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide, mixt. with 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl di-(9Z)-9-octadecenoate (9CI) (CA INDEX NAME)

CM 1

CRN 153312-64-2
CMF C35 H74 N O3 . Br

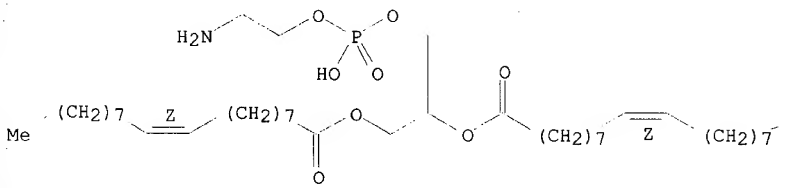


CM 2

CRN 2462-63-7
CMF C41 H78 N O8 P

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 11
ACCESSION NUMBER: 1998:249878 CAPLUS
DOCUMENT NUMBER: 129:12373
TITLE: Transfection of primary tumor cells and tumor cell lines with plasmid DNA/lipid complexes
AUTHOR(S): Stopeck, Alison T.; Hersh, Evan M.; Brailey, Jacqueline L.; Clark, Paul R.; Norman, Jon; Parker, Suezanne E.
CORPORATE SOURCE: Arizona Cancer Center, Tucson, AZ, 85724-5024, USA
SOURCE: Cancer Gene Therapy (1998), 5(2), 119-126
CODEN: CGTHEG; ISSN: 0929-1903
PUBLISHER: Appleton & Lange
DOCUMENT TYPE: Journal
LANGUAGE: English

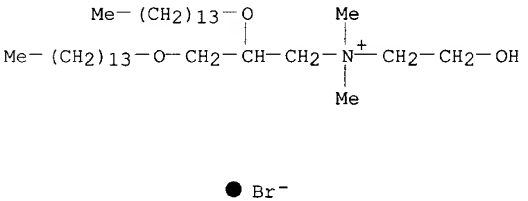
Searched by Barb O'Bryen, STIC 308-4291

AB Cancer vaccines that utilize genetically modified tumor cells require gene transfer methods capable of producing immunostimulatory doses of transgenes from fresh or short-term cultures of human tumor cells. Our studies optimize in vitro transfection of primary tumor cells using cationic lipids and a plasmid encoding the gene for human interleukin-2 (IL-2). Established tumor cell lines produced 10- to 100-fold more IL-2 than did fresh or short-term tumor cultures as measured by enzyme-linked immunoabsorbent anal. Importantly, transfection of primary tumor cells produced immunostimulatory levels of IL-2 as detd. by increased thymidine incorporation by autologous peripheral blood mononuclear cells and lymphokine-activated killer cell activity. IL-2 secretion by tumor cells persisted for at least 30 days post-transfection and was unaffected by freeze thawing or irradn. to 8000 rads. Multiple solid tumor types were successfully transfected, but normal blood mononuclear cells and leukemic blasts were resistant to transfection. Enzyme-linked immunoabsorbent anal. of the amt. of IL-2 secreted into the medium by transfected tumor cells correlated with the percentage of tumor cells expressing intracellular IL-2 as measured by flow cytometry. Plasmids utilizing a cytomegalovirus promoter yielded superior transfection efficiencies compared with plasmids contg. a Rous sarcoma virus promoter. These results suggest that a clin. vaccine trial using autologous tumor cells genetically modified to secrete IL-2 is feasible in patients with solid tumors.

IT **153312-64-2**, DMRIE
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(primary tumor cell and tumor cell line transfection with IL-2-encoding plasmid DNA/cationic lipid complexes)

RN 153312-64-2 CAPLUS

CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 12 OF 37 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 12

ACCESSION NUMBER: 1997:300574 CAPLUS
DOCUMENT NUMBER: 127:32672
TITLE: Phase I study of immunotherapy of hepatic metastases of colorectal carcinoma by direct gene transfer of an allogeneic histocompatibility antigen, HLA-B7
AUTHOR(S): Rubin, J.; Galanis, E.; Pitot, H. C.; Richardson, R. L.; Burch, P. A.; Charboneau, J. W.; Reading, C. C.; Lewis, B. D.; Stahl, S.; Akporiaye, E. T.; Harris, D. T.
CORPORATE SOURCE: Div. Med. Oncology, Mayo Clinic and Mayo Foundation, Rochester, MN, USA
SOURCE: Gene Therapy (1997), 4(5), 419-425
CODEN: GETHEC; ISSN: 0969-7128
PUBLISHER: Stockton
DOCUMENT TYPE: Journal
LANGUAGE: English

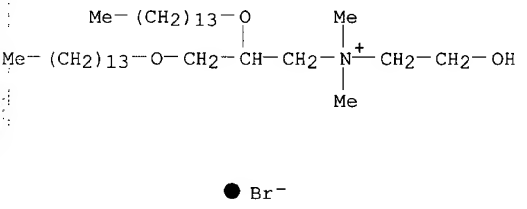
Searched by Barb O'Bryen, STIC 308-4291

AB The authors have completed a phase I study to test feasibility and toxicity of immunotherapy of hepatic metastases from colorectal carcinoma by direct gene transfer of HLA-B7, a MHC class I gene. Eligible patients were HLA-B7 neg., immunocompetent by PHA lymphocyte stimulation and had at least two measurable hepatic lesions on CT scan for measurement of response of the injected lesion, as well as evaluation of possible distant response. Under ultrasonog. guidance the hepatic lesions were injected with Allovectin-7, a liposomal vector contg. the combination of the HLA-B7 gene with .beta.2-microglobulin formulated with the lipid DMRIE-DOPE. Eligible patients were injected on two schedules. On the first schedule patients received an injection on day 1 and the injected lesion was biopsied to det. transfection every 2 wk for 8 wk. Doses were escalated from 10 .mu.g to 50 .mu.g to 250 .mu.g with three patients treated at each level. The second schedule included multiple injections of 10 .mu.g. Three patients received injection on days 1 and 15. Three patients received injections on days 1, 15 and 29. A total of 15 patients have completed treatment. The plasmid DNA was detected in 14 of 15 patients (93%) by PCR. In five of 15 patients (33%) mRNA was also detected. The HLA-B7 protein was detected in five of eight patients (63%) by immunohistochem. and in seven of 14 patients (50%) tested by fluorescence activated cell sorting (FACS) anal. There has been no serious toxicity directly attributable to Allovectin-7. The results suggest that liposomal gene transfer by direct injection is feasible and non-toxic. Further studies will be necessary to establish the therapeutic efficacy.

IT **153312-64-2**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene transfer of allogeneic HLA-B7 to human hepatic metastases of colorectal carcinoma)

RN 153312-64-2 CAPLUS

CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



L54 ANSWER 13 OF 37 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 13

ACCESSION NUMBER:	1995:468608 CAPLUS
DOCUMENT NUMBER:	123:102768
TITLE:	Plasmids suitable for gene therapy
INVENTOR(S):	Nabel, Gary J.; Nabel, Elizabeth G.; Lew, Denise; Marquet, Magda
PATENT ASSIGNEE(S):	Vical Inc., USA; Regents of the University of Michigan
SOURCE:	PCT Int. Appl., 50 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9429469	A2	19941222	WO 1994-US6069	19940527
WO 9429469	A3	19950323		

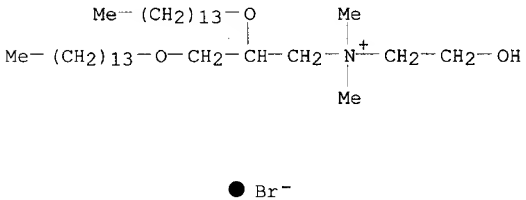
Searched by Barb O'Bryen, STIC 308-4291

W: CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
EP 702722 A1 19960327 EP 1994-919290 19940527
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
US 5910488 A 19990608 US 1995-564313 19951201
PRIORITY APPLN. INFO.: US 1993-74344 19930607
WO 1994-US6069 19940527

AB The invention provides vectors adapted for use in transferring into tissue or cells of an organism genetic mater. encoding one or more cistrons capable of expressing one or more immunogenic or therapeutic peptides and related methods. Prepn. of a HLA-B7-encoding plasmid that contains the origin of replication of pBR322, the RSV LTR promoter, SV40 polyadenylation signal, etc., methods for transfection using cationic lipid formulations comprising DMRIE/DOPE, and its use in gene therapy are also described.

IT **153312-64-2**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(transfection of host cells with recombinant plasmids for expression of HLA-B7 and .beta.-2 microglobulin in gene therapy facilitated by)

RN 153312-64-2 CAPLUS
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)

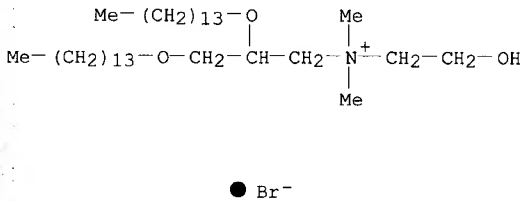


L54 ANSWER 14 OF 37 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:594655 CAPLUS
DOCUMENT NUMBER: 137:159311
TITLE: Polymer combinations that result in stabilized aerosols for gene delivery to the lungs
INVENTOR(S): Zou, Yiyu; Perez-Soler, Roman
PATENT ASSIGNEE(S): Board of Regents, The University of Texas System, USA
SOURCE: PCT Int. Appl., 136 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002060412	A2	20020808	WO 2002-US2909	20020201

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,

BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2002187105 A1 20021212 US 2002-61444 20020201
PRIORITY APPLN. INFO.: US 2001-266174P P 20010201
AB The use of non-viral delivery of therapeutically effective compns. through aerosols for therapy or research purpose has been limited by low efficiency mainly caused by an inefficient delivery system and destruction of formulation (gene and/or delivery system) by aerosol shearing power. This invention develops formulations that are established polymer combination formulations. The formulations are highly efficient in delivering genes in vivo through aerosols and are able to protect the delivered gene from the destruction by aerosol shearing power.
IT **153312-64-2**, Dmrie
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(polymer combinations that result in stabilized aerosols for gene delivery to the lungs)
RN 153312-64-2 CAPLUS
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



L54 ANSWER 15 OF 37 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:798084 CAPLUS
DOCUMENT NUMBER: 135:348865
TITLE: Compositions and methods for in vivo delivery of polynucleotide-based therapeutics
INVENTOR(S): Hartikka, Jukka; Sukhu, Loretta; Manthorpe, Marston
PATENT ASSIGNEE(S): Vical Incorporated, USA
SOURCE: PCT Int. Appl., 176 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

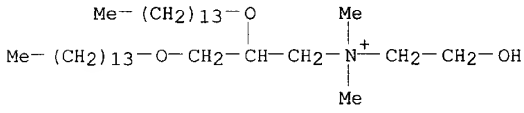
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001080897	A2	20011101	WO 2001-US12975	20010423
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
US 2002019358	A1	20020214	US 2001-839574	20010423
EP 1278551	A2	20030129	EP 2001-928741	20010423
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				

PRIORITY APPLN. INFO.: US 2000-198823P P 20000421
US 2000-253153P P 20001128
WO 2001-US12975 W 20010423
AB The present invention relates to pharmaceutical compns. and methods to improve expression of exogenous polypeptides into vertebrate cells in

vivo, utilizing delivery of polynucleotides encoding such polypeptides. More particularly, the present invention provides the use of salts, in particular sodium and potassium salts of phosphate, in aq. soln., and auxiliary agents, in particular detergents and surfactants, in pharmaceutical compns. and methods useful for direct polynucleotide-based polypeptide delivery into the cells of vertebrates.

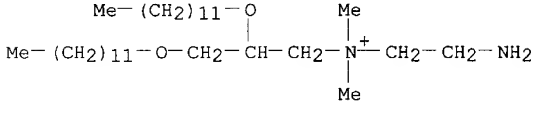
IT **153312-64-2**, Dmrie **208040-06-6**, Gap dlrie
299207-54-8, Gap-dmorie
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(compns. and methods for in vivo delivery of polynucleotide-based therapeutics)

RN 153312-64-2 CAPLUS
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



● Br^-

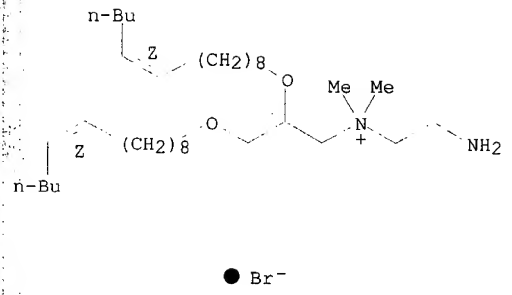
RN 208040-06-6 CAPLUS
CN 1-Propanaminium, N-(2-aminoethyl)-2,3-bis(dodecyloxy)-N,N-dimethyl-, bromide (9CI) (CA INDEX NAME)



● Br^-

RN 299207-54-8 CAPLUS
CN 1-Propanaminium, N-(2-aminoethyl)-N,N-dimethyl-2,3-bis[(9Z)-9-tetradecenyloxy]-, bromide (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L54 ANSWER 16 OF 37 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:545519 CAPLUS
DOCUMENT NUMBER: 135:142202
TITLE: Improved DNA vaccines for livestock
INVENTOR(S): Audonnet, Jean-Christophe Francis; Fischer, Laurent Bernard; Barzu-le-Roux, Simona
PATENT ASSIGNEE(S): Merial, Fr.
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001052888	A2	20010726	WO 2001-FR187	20010119
WO 2001052888	A3	20011220		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2804028	A1	20010727	FR 2000-798	20000121
US 2002058021	A1	20020516	US 2001-760574	20010116
EP 1248650	A2	20021016	EP 2001-907651	20010119
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001007767	A	20021112	BR 2001-7767	20010119

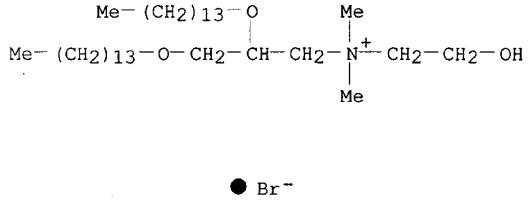
PRIORITY APPLN. INFO.:

FR 2000-798	A	20000121
US 2000-193126P	P	20000330
WO 2001-FR187	W	20010119

OTHER SOURCE(S): MARPAT 135:142202

AB The invention concerns a DNA vaccine against a pathogen affecting livestock, in particular cattle and swine, comprising a plasmid contg. a nucleotide sequence coding for an immunogen of a pathogen of the animal species concerned, in conditions enabling the expression in vivo of said sequence, and a cationic lipid contg. a quaternary ammonium salt, of formula R1-O-CH2-CH(OR1)-CH2-N+(CH3)2-R2 X-, wherein: R1 is a linear aliph. radical, satd. or unsatd., having 12 to 18 carbon atoms; R2 is another aliph. radical, contg. 2 or 3 carbon atoms; and X is a hydroxyl or amine group, said lipid being preferably DMRIE.

IT **153312-64-2**, Dmrie
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(improved DNA vaccines for livestock)
RN 153312-64-2 CAPLUS
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



L54 ANSWER 17 OF 37 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:168152 CAPLUS
DOCUMENT NUMBER: 134:221435
TITLE: Prevention of myocarditis, abortion and intrauterine infection associated with porcine circovirus-2
INVENTOR(S): Ellis, John Albert; Allan, Gordon Moore; Meehan, Brian; Clark, Edward; Haines, Deborah; Hassard, Lori; Harding, John; Charreyre, Catherine Elisabeth; Chappuis, Gilles Emile; Krakowka, George Steve; Audonnet, Jean-Christophe Francis; McNeilly, Francis
PATENT ASSIGNEE(S): Merial, Fr.; University of Saskatchewan; The Queen's University of Belfast
SOURCE: PCT Int. Appl., 133 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001016330	A2	20010308	WO 2000-EP8781	20000828
WO 2001016330	A3	20020808		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6517843	B1	20030211	US 2000-583350	20000531
BR 2000014155	A	20020507	BR 2000-14155	20000828
EP 1246920	A2	20021009	EP 2000-960628	20000828
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

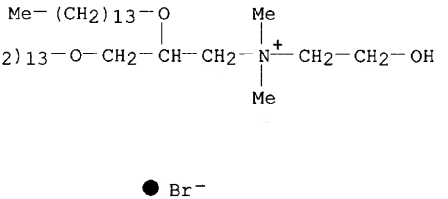
PRIORITY APPLN. INFO.:
US 1999-151564P P 19990831
US 2000-583350 A 20000531
WO 2000-EP8781 W 20000828

AB The invention is based on the discovery that porcine circovirus (PCV-2) is a causative agent of myocarditis, abortion and intrauterine infection, as

well as post-weaning multisystemic wasting syndrome in pigs. Thus, immunol. compns. contg. the recombinant poxvirus for inducing an immunol. response in aa host animal to which the immunol. compn. is administered. Also described are methods of treating or preventing disease caused by PCV-2 by administering the immunol. compns. of the invention to an animal in need of treatment or susceptible to infection by PCV-2. Such immunol. compns. comprise (1) attenuated or inactivated strains of PCV-2, (2) plasmid vectors expressing open reading frames of PCV-2 and vaccination of pigs with DNA formulated with DMRIE, DMRIE-DOPE, or carbomer adjuvants, and (3) a recombinant poxvirus, such as the canarypox virus (Rentschler strain) contg. foreign DNA encoding the major capsid virus or ORF1 or ORF2 from PCV-2.

IT **153312-64-2**, DMRIE
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adjuvant; prevention of myocarditis, abortion and intrauterine infection assocd. with porcine circovirus-2)

RN 153312-64-2 CAPLUS
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



L54 ANSWER 18 OF 37 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:114958 CAPLUS
DOCUMENT NUMBER: 134:168319
TITLE: Periodic structures comprising lipids, polyelectrolytes, and structure-inducing soluble oligovalent linkers, and biological use thereof
INVENTOR(S): Cevc, Gregor; Huebner, Stefan
PATENT ASSIGNEE(S): Idea Ag, Germany
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001010413	A2	20010215	WO 2000-EP7546	20000803
WO 2001010413	A3	20010816		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

JP 2003506398	T2	20030218	JP 2001-514933	20000803

PRIORITY APPLN. INFO.: DE 1999-19936665 A 19990804

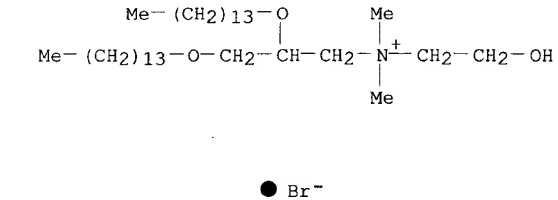
WO 2000-EP7546 W 20000803

AB This invention describes a method for prepg. pharmaceutically usable compns. comprising periodic structures consisting of polyelectrolytes sandwiched between lipid aggregates having at least one charged component which is characterized in that a suspension of non-periodic, preferably mono- or bilayer like, lipid aggregates, a soln. of polyelectrolyte mols., and a soln. of oligovalent linkers are sep. made and then mixed to form said periodic structures, the simultaneous presence of said components catalyzing the formation of controlling the rate of formation of said periodic structures comprising at least one layer of lipid component assocd. with a layer of polyelectrolyte mols.

IT **153312-64-2**, Dmrie
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(periodic structures comprising lipids, polyelectrolytes, and structure-inducing sol. oligovalent linkers, and biol. use thereof)

RN 153312-64-2 CAPLUS

CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



L54 ANSWER 19 OF 37 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:64121 CAPLUS
DOCUMENT NUMBER: 134:136654
TITLE: Feline calicivirus genes and vaccines, in particular recombined vaccines
INVENTOR(S): Audonnet, Jean-Christophe Francis; Baudu, Philippe Guy Nicolas; Brunet, Sylvie Claudine
PATENT ASSIGNEE(S): Merial, Fr.
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001005934	A2	20010125	WO 2000-FR2051	20000713
WO 2001005934	A3	20010426		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2796396	A1	20010119	FR 1999-9421	19990716
FR 2796397	A1	20010119	FR 2000-1761	20000211

AU 2000065765	A5	20010205	AU 2000-65765	20000713
BR 2000012512	A	20020402	BR 2000-12512	20000713
EP 1228193	A2	20020807	EP 2000-953243	20000713

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, IE, SI, LT, LV, FI, RO, MK, CY, AL

PRIORITY APPLN. INFO.:
FR 1999-9421 A 19990716
FR 2000-1761 A 20000211
WO 2000-FR2051 W 20000713

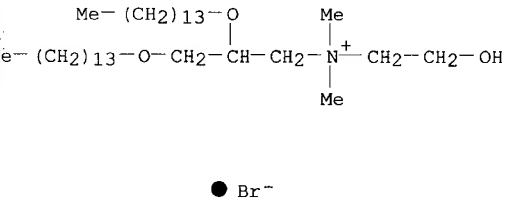
OTHER SOURCE(S): MARPAT 134:136654

AB The invention concerns the sequence of the capsid gene and a corresponding cDNA sequence, of a dominant FCV strain called FCV 431. The invention also concerns the capsid gene sequence and the cDNA sequence of a complementary strain called G1. The cDNA sequences can be incorporated in expression vectors for prepg. immunogenic formulations and recombined vaccines or subunits providing vaccination against the feline calicivirus disease.

IT **153312-64-2**, Dmrie
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(adjuvant; feline calicivirus genes and vaccines)

RN 153312-64-2 CAPLUS

CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



L54 ANSWER 20 OF 37 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:791879 CAPLUS
DOCUMENT NUMBER: 135:335117
TITLE: Immunological adjuvants containing Hemagglutinating virus-containing charged liposomes, and manufacture thereof
INVENTOR(S): Honda, Kazuo; Kaneda, Yasushi; Shiozaki, Koichi
PATENT ASSIGNEE(S): Chemo-Sero-Therapeutic Research Institute, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001302541	A2	20011031	JP 2000-128670	20000428

PRIORITY APPLN. INFO.: JP 2000-128670 20000428

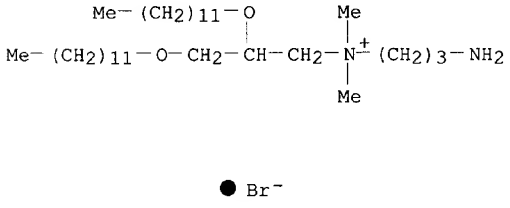
AB The invention relates to an immunol. adjuvant having immunostimulating effect for low-immunogenic peptide, wherein the adjuvant is a charged liposome consisting of a Sendai virus (Hemagglutinating virus of Japan, HVJ virus) or its envelop glycoprotein, and a lipid component. A HIV-V3 peptide-contg. anionic liposome was prepd. from dimethylaminoethane carbamyl cholesterol, phosphatidylethanolamine, egg yolk

phosphatidylcholine, cholesterol, inactivated HVJ virus, and HIV-V3 peptide, and its booster effect was examd. in guinea pigs primarily immunized with HIV-HBc (hepatitis B virus core antigen).

IT **182919-20-6**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (charged liposomes contg. Hemagglutinating virus and lipids as immunol. adjuvants)

RN 182919-20-6 CAPLUS

CN 1-Propanaminium, N-(3-aminopropyl)-2,3-bis(dodecyloxy)-N,N-dimethyl-, bromide (9CI) (CA INDEX NAME)



L54 ANSWER 21 OF 37 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:900790 CAPLUS
DOCUMENT NUMBER: 134:55493
TITLE: Porcine circovirus vaccine
INVENTOR(S): Audonnet, Jean-christophe Francis; Bublot, Michel; Perez, Jennifer Maria; Charreyre, Catherine Elisabeth
PATENT ASSIGNEE(S): Merial, Fr.
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000077188	A2	20001221	WO 2000-EP5611	20000608
WO 2000077188	A3	20010531		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1185659	A2	20020313	EP 2000-935220	20000608
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000011733	A	20020723	BR 2000-11733	20000608
JP 2003502303	T2	20030121	JP 2001-503633	20000608

PRIORITY APPLN. INFO.: US 1999-138352P P 19990610
WO 2000-EP5611 W 20000608

OTHER SOURCE(S): MARPAT 134:55493

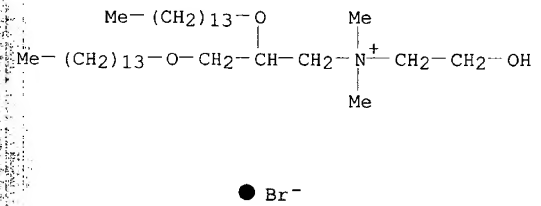
AB The invention relates to immunogenic prepns. or vaccines comprising, on the one hand, a plasmid vector encoding and expressing a gene from porcine circovirus (PCV), in particular selected from the group consisting of ORF1 of PCV-2, ORF2 of PCV-2, ORF1 of PCV-1 and ORF2 of PCV-1, and , on the

other hand, an element capable of increasing the immune response directed against the product of expression of the gene, which can be a carbomer, a porcine cytokine, e.g. GM-CSF or a cationic lipid of formula (I), in which R1 is a satd. or unsatd. linear aliph. radical having from 12 to 18 carbon atoms, R2 is another aliph. radical comprising from 2 to 3 carbon atoms, and X is a hydroxyle or amine group. The cationic lipid can be DMRIE, possibly coupled with DOPE. Vaccines contg. plasmid vector encoding and expressing a gene from porcine circovirus were prepd. and tested against PMWS.

IT **153312-64-2**, DMRIE
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vaccine comprising, cationic lipid or neutral lipid; porcine circovirus vaccine)

RN 153312-64-2 CAPLUS

CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



L54 ANSWER 22 OF 37 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:900679 CAPLUS
DOCUMENT NUMBER: 134:55491
TITLE: DNA vaccines against Paramyxoviridae for pets and game animals and their delivery in liposomes containing cationic lipids
INVENTOR(S): Fischer, Laurent Jean-Charles; Barzu-le, Roux Simona; Audonnet, Jean-Christophe Francis
PATENT ASSIGNEE(S): Merial, Fr.
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000077043	A2	20001221	WO 2000-FR1592	20000608
WO 2000077043	A3	20010719		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2794648	A1	20001215	FR 1999-7604	19990610
BR 2000011732	A	20020305	BR 2000-11732	20000608
EP 1185662	A2	20020313	EP 2000-940474	20000608
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO
JP 2003502345 T2 20030121 JP 2001-503899 20000608
PRIORITY APPLN. INFO.: FR 1999-7604 A 19990610
US 1999-144490P P 19990719
WO 2000-FR1592 W 20000608

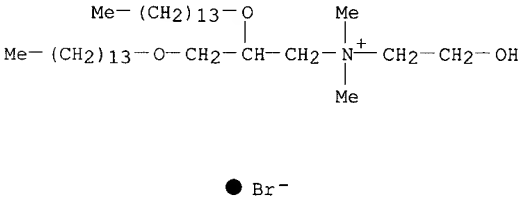
OTHER SOURCE(S): MARPAT 134:55491

AB The invention aims at improving the efficacy and protection induced by DNA vaccination against viruses of the family of Paramyxoviridae and against the herpes virus, in pets and sport animals. The improvement of DNA vaccination is achieved either by formulating the vaccine with a cationic lipid contg. a quaternary ammonium salt, DMRIE, or by modifications in the nucleotide sequence coding for the antigen of interest in particular of deletions of the fragment of the nucleotide sequence coding for the transmembrane domain of the antigen of interest, and/or insertions of introns and/or insertions of nucleotide sequences coding for the signal peptides, or by adding GM-CSF, or by combinations thereof. The invention also concerns the resulting vaccines. A series of expression vectors for antigen genes of canine distemper virus and felid, canid, and equid herpes viruses that used the signal sequence of a tissue plasminogen activator gene were constructed by std. methods. In some cases, derivs. lacking the transmembrane domain were used to improve secretion of the extracellular domain. Expression vectors also carrying the genes for cytokines, esp. colony-stimulating factor 2 were also constructed. Use of genes for colony-stimulating factor 2 derived from the target host is demonstrated. A combination of vectors carrying genes for the fusion protein and hemagglutinin of canine distemper virus completely protected a group of five dogs challenged with the virus.

IT **153312-64-2**, DMRIE
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in liposomes for delivery of DNA vaccines; DNA vaccines against Paramyxoviridae for pets and game animals and their delivery in liposomes contg. cationic lipids)

RN 153312-64-2 CAPLUS

CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



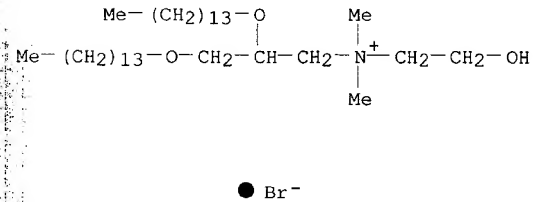
L54 ANSWER 23 OF 37 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:679109 CAPLUS
DOCUMENT NUMBER: 132:164839
TITLE: Adjuvants for plasmid DNA vaccines
AUTHOR(S): Norman, Jon; Hartikka, Jukka; Strauch, Pamela; Manthorpe, Marston
CORPORATE SOURCE: Vical Inc., San Diego, CA, USA
SOURCE: Methods in Molecular Medicine (2000), 29, 185-196
CODEN: MMMEFN
PUBLISHER: Humana Press Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 38 refs. discussing the effects of the co-injection of

bupivacaine (BP), polyvinyl pyrollidone (PVP), or DMRIE:DOPE cationic liposomes on plasmid DNA-mediated luciferase gene expression and antibody responses to influenza nucleoprotein (NP) antigen.

IT **153312-64-2**, DMRIE
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DMRIE/DOPE liposomes contg.; adjuvants for plasmid DNA vaccines)

RN 153312-64-2 CAPLUS
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 24 OF 37 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:355754 CAPLUS
DOCUMENT NUMBER: 131:18016
TITLE: Treatment of cancer using cytokine-expressing polynucleotides and compositions therefor
INVENTOR(S): Horton, Holly; Parker, Suezanne; Manthorpe, Marston; Felgner, Philip
PATENT ASSIGNEE(S): Vical, Inc., USA
SOURCE: PCT Int. Appl., 188 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9926663	A2	19990603	WO 1998-US24830	19981120
WO 9926663	A3	20000106		
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2309766	AA	19990603	CA 1998-2309766	19981120
EP 1032428	A2	20000906	EP 1998-960333	19981120
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001523480	T2	20011127	JP 2000-521864	19981120

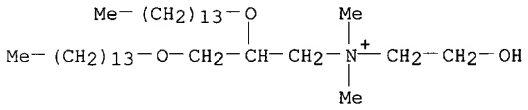
PRIORITY APPLN. INFO.:
US 1997-67087P P 19971120
US 1998-79914P P 19980330
US 1998-100820P P 19980915
WO 1998-US24830 W 19981120

AB The present invention provides a pharmaceutical compn., comprising a non-infectious, non-integrating polynucleotide construct comprising a polynucleotide encoding an interferon .omega. and one or more cationic compds. The present invention also provides methods of treating cancer in a mammal, comprising administering into a tissue of the mammal a

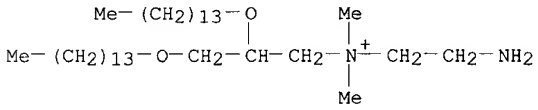
non-infectious, non-integrating polynucleotide construct comprising a polynucleotide encoding a cytokine. In addn., the present invention also relates to the methodol. for selective transfection of malignant cells with polynucleotides expressing therapeutic or prophylactic mols. in intracavity tumor bearing mammals. More specifically, the present invention provides a methodol. for the suppression of an intra-cavity dissemination of malignant cells, such as i.p. dissemination.

IT **153312-64-2 154486-25-6 182919-20-6**
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(gene therapy of cancer using cytokine-expressing polynucleotides)

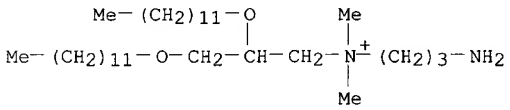
RN 153312-64-2 CAPLUS
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



RN 154486-25-6 CAPLUS
CN 1-Propanaminium, N-(2-aminoethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



RN 182919-20-6 CAPLUS
CN 1-Propanaminium, N-(3-aminopropyl)-2,3-bis(dodecyloxy)-N,N-dimethyl-, bromide (9CI) (CA INDEX NAME)



L54 ANSWER 25 OF 37 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:621321 CAPLUS
DOCUMENT NUMBER: 129:235638

TITLE: Construction of cationic lipid complex-polynucleotides-contg.liposomes for gene delivery to mucosal epithelium for immunization or therapeutic purposes
INVENTOR(S): Davis, Heather Lynn; Jessee, Joel; Gebeyehu, Gulilat
PATENT ASSIGNEE(S): Can.
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

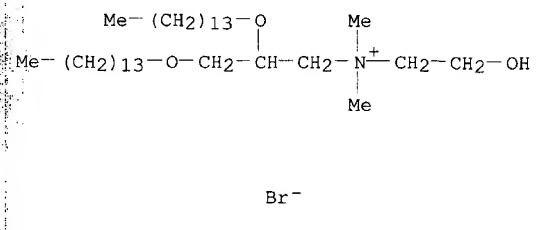
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9840499	A1	19980917	WO 1997-US3421	19970310
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9719871	A1	19980929	AU 1997-19871	19970310

PRIORITY APPLN. INFO.: WO 1997-US3421 19970310

AB Disclosed are compns. and method for transfecting mammalian mucosal epithelia with nucleic acid/cationic lipid complexes. The nucleic acid/cationic lipid complexes may be administered, for example, intranasally or directly into the lungs. The best results are obtained when the lipid mixed with the max. amt. of DNA that it can complex. Thus, cationic lipids are complexed with a polynucleotides coding for immunogenic antigens in mice. Hybridomas are constructed by fusing B-lymphocytes with myeloma cells, and pos. clones are selected which produce anti-immunogen antibody. Suitable cationic lipids include DOTMA, DOTAP, and DORI-esters. Neutral lipids that can be used include lecithins, phosphotidylethanolamine, phosphatidylethanolamines (e.g. DOPE, OPPE), and distearoylphosphatidylethanolamine. Cationic sterol derivs., such as DC-Chol can also be used. Polyclonal and monoclonal antibodies and antisense oligonucleotides are also claimed effective to gene therapy. The method is tested in a mouse system.

IT **153312-64-2**, Dmrie **189203-05-2**, Dmrie-C **212893-21-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(construction of cationic lipid complex-polynucleotides-contg.liposomes for gene delivery to mucosal epithelium for immunization or therapeutic purposes)

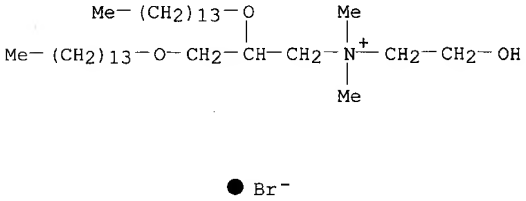
RN 153312-64-2 CAPLUS
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



RN 189203-05-2 CAPLUS
CN Cholest-5-en-3-ol (3.beta.)-, mixt. with N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-1-propanaminium bromide (9CI) (CA INDEX NAME)

CM 1

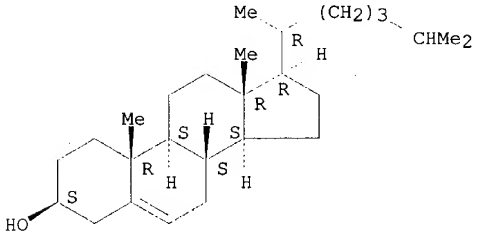
CRN 153312-64-2
CMF C35 H74 N O3 . Br



CM 2

CRN 57-88-5
CMF C27 H46 O

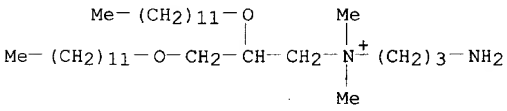
Absolute stereochemistry.



RN 212893-21-5 CAPLUS
CN 1-Propanaminium, N-(3-aminopropyl)-2,3-bis(dodecyloxy)-N,N-dimethyl-, mixt. with (Z,Z)-1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl di-9-octadecenoate (9CI) (CA INDEX NAME)

CM 1

CRN 191980-99-1
CMF C32 H69 N2 O2

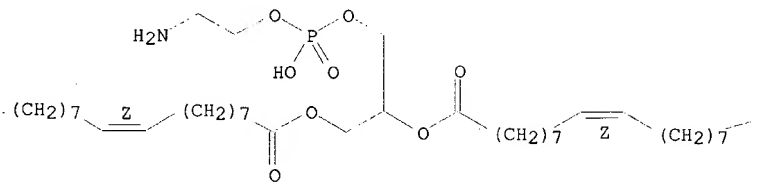


CM 2

CRN 2462-63-7
CMF C41 H78 N O8 P

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 26 OF 37 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:517159 CAPLUS
DOCUMENT NUMBER: 129:188218
TITLE: Lipid-mediated gene transfer of viral IL-10 prolongs vascularized cardiac allograft survival by inhibiting donor-specific cellular and humoral immune responses
AUTHOR(S): DeBruyne, L. A.; Li, K.; Chan, S. Y.; Qin, L.; Bishop, D. K.; Bromberg, J. S.
CORPORATE SOURCE: Dep. Surg., Univ. Michigan Med. Cent., Ann Arbor, MI, 48109, USA
SOURCE: Gene Therapy (1998), 5(8), 1079-1087
CODEN: GETHEC; ISSN: 0969-7128
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The gene encoding the immunosuppressive cytokine viral interleukin-10 (vIL-10) was introduced into BALB/c (H-2d) vascularized cardiac allografts by perfusing the graft vasculature with DNA-liposome complexes, utilizing the exptl. cationic lipid .gamma.AP DLRIE/DOPE and a plasmid encoding vIL-10 under the control of the HCMVie promoter. The DNA to lipid ratio and DNA dose were crit. factors in obtaining optimal biol. effects. Gene transfer of vIL-10 with a 3:1 DNA to lipid wt. ratio using 375 .mu.g DNA significantly prolonged allograft survival in MHC-mis-matched C57BL/6 (H-2b) recipients (16.00 days) compared with both unmodified allografts (8.14 days) and vIL-10 anti-sense controls (8.28 days). Enhanced graft survival was specific to vIL-10 expression since treatment with anti-sense plasmid or anti-vIL-10 monoclonal antibody (mAb) abrogated the effect. Prolonged survival was assocd. with a novel histol. characterized by a moderate mono-nuclear infiltrate, edema, and diffuse fibrillar/collagen deposition in the interstitium. Despite these morphol. changes, myocytes remained viable and vessels were patent. Limiting diln. anal. revealed transient infiltration of IL-2 secreting, donor-reactive, helper T

lymphocytes (HTL) and cytotoxic T lymphocytes (CTL) in vIL-10 expressing grafts on day 7, the decreased significantly by day 14. Similarly, vIL-10 gene transfer inhibited the accumulation of donor-specific HTL and CTL in the spleen, compared with antisense controls. Prolonged survival was also assocd. with a marked decrease in IgM and IgG alloantibody prodn., with little to no IgG isotype switching. These results show that viral IL-10 gene transfer inhibits graft rejection in a clin. relevant model by inhibiting donor-specific cellular and humoral immune responses.

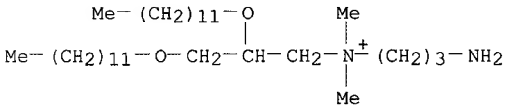
IT **200357-85-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipid-mediated gene transfer of viral IL-10 prolongs vascularized cardiac allograft survival)

RN 200357-85-3 CAPLUS

CN 1-Propanaminium, N-(3-aminopropyl)-2,3-bis(dodecyloxy)-N,N-dimethyl-, bromide, mixt. with 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl di-(9Z)-9-octadecenoate (9CI) (CA INDEX NAME)

CM 1

CRN 182919-20-6
CMF C32 H69 N2 O2 . Br

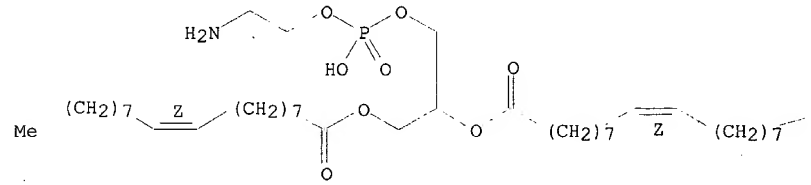


CM 2

CRN 2462-63-7
CMF C41 H78 N O8 P

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

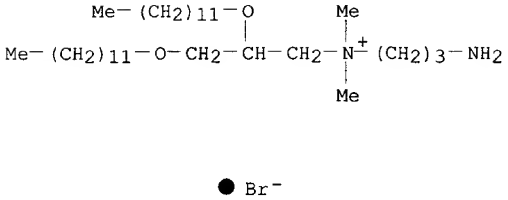
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 27 OF 37 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:473805 CAPLUS
DOCUMENT NUMBER: 127:175118
TITLE: Development of improved vectors for DNA-based immunization and other gene therapy applications
AUTHOR(S): Norman, Jon A.; Hobart, Peter; Manthorpe, Marston; Felgner, Phil; Wheeler, Carl
CORPORATE SOURCE: Vical Inc., San Diego, CA, 92121, USA
SOURCE: Vaccine (1997), 15(8), 801-803
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Optimizing gene expression and delivery are necessary steps in the prodn. of vectors for DNA-based immunization as well as for other gene therapy applications. A mouse muscle/reporter gene assay system was used to systematically improve a plasmid DNA vector. The optimized vector VR1255 contained: (1) CMV promoter and enhancer; (2) CMV IE Intron A; (3) kanamycin resistance gene; (4) deleted SV40 origin of replication; (5) optimized lux coding region; and (6) a minimal synthetic terminator from the rabbit beta globin gene, mRBG. The vector VR1255 expressed 137 times greater than an earlier prototype RSV-based vector. For plasmid vector delivery into nonmuscle tissues, a recently synthesized cationic lipid, GAP-DLRIE, was found to greatly enhance the uptake and expression of plasmid DNA by 100-fold when instilled into the mouse lung. The time-course of CAT expression with GAP-DLRIE indicated that peak expression occurs 2-5 days after intranasal administration and expression diminished to about one-third the peak value by day 21. This cationic lipid may be useful for immunization by pulmonary and perhaps other nonmuscle routes.

IT **182919-20-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(development of improved vectors for DNA-based immunization and other gene therapy applications)

RN 182919-20-6 CAPLUS
CN 1-Propanaminium, N-(3-aminopropyl)-2,3-bis(dodecyloxy)-N,N-dimethyl-, bromide (9CI) (CA INDEX NAME)



L54 ANSWER 28 OF 37 USPATFULL

ACCESSION NUMBER:	2003:40418 USPATFULL
TITLE:	Reduction of porcine circovirus-2 viral load with inactivated PCV-2
INVENTOR(S):	Ellis, John Albert, Saskatoon, CANADA Moore, Gordon Allan, Belfast, UNITED KINGDOM Meehan, Brian, Belfast, UNITED KINGDOM Clark, Edward, Saskatoon, CANADA Haines, Deborah, Saskatoon, CANADA Hassard, Lori, Saskatoon, CANADA Harding, John, Humboldt, CANADA Charreyre, Catherine Elisabeth, Saint-Laurent de Mure, FRANCE Chappuis, Gilles Emile, Lyons, FRANCE Krakowka, George Steve, Columbus, OH, United States Audonnet, Jean-Christophe Francis, Lyons, FRANCE McNeilly, Francis, Newtownards, UNITED KINGDOM
PATENT ASSIGNEE(S):	Merial, Lyons, FRANCE (non-U.S. corporation) University of Saskatchewan, Saskatoon, CANADA (non-U.S. corporation) The Queen's University of Belfast, Belfast, UNITED KINGDOM (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6517843	B1	20030211	
APPLICATION INFO.:	US 2000-583350		20000531	(9)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1999-151564P	19990831	(60)

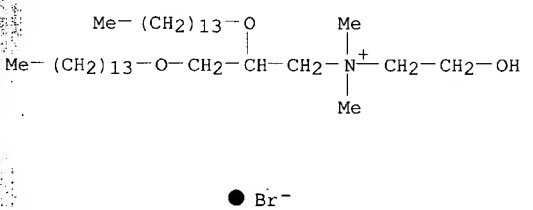
DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Housel, James
ASSISTANT EXAMINER:	Foley, Shanon
LEGAL REPRESENTATIVE:	Frommer Lawrence & Haug, LLP, Frommer, William S., Kowalski, Thomas J.
NUMBER OF CLAIMS:	6
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	8 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT:	1927

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Porcine circovirus-2 (PCV-2) is a recently identified agent wherein the potential spectrum of PCV-2-associated disease has been expanded by evidence of vertical and sexual transmission and associated reproductive failure in swine populations. PCV-2 was isolated from a litter of aborted piglets from a farm experiencing late term abortions and stillbirths. Severe, diffuse myocarditis was present in one piglet associated with extensive immunohistochemical staining for PCV-2 antigen. Variable amounts of PCV-2 antigen were also present in liver,

lung and kidney of multiple fetuses. Inoculation of female pigs with a composition including an immunogen from PCV-2 or an epitope of interest from such an immunogen or with a vector expressing such an immunogen or epitope of interest prior to breeding, such as within the first five weeks of life, or prior to the perinatal period, or repeatedly over a lifetime, or during pregnancy, such as between the 6.sup.th and 8.sup.th and/or the 10.sup.th and 13.sup.th weeks of gestation, can prevent myocarditis, abortion and intrauterine infection associated with porcine circovirus-2. In addition, innoculation of male and/or female pigs with the aforementioned compositions can be carried out to prevent transmission of PCV-2 from male to female (or vice versa) during mating. Thus, the invention involves methods and compositions for preventing myocarditis, abortion and intrauterine infection associated with porcine circovirus-2.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **153312-64-2**, DMRIE
(adjuvant; prevention of myocarditis, abortion and intrauterine infection assocd. with porcine circovirus-2)
RN 153312-64-2 USPATFULL
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



L54 ANSWER 29 OF 37 USPATFULL
ACCESSION NUMBER: 2002:329426 USPATFULL
TITLE: Polymer combinations that result in stabilized aerosols for gene delivery to the lungs
INVENTOR(S): Zou, Yiyu, Bronx, NY, UNITED STATES
Perez-Soler, Roman, New York, NY, UNITED STATES

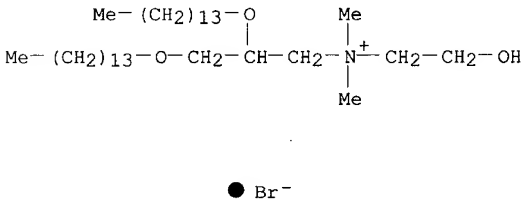
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002187105	A1	20021212
APPLICATION INFO.:	US 2002-61444	A1	20020201 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-266174P	20010201 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: FULBRIGHT & JAWORSKI L.L.P., A REGISTERED LIMITED LIABILITY PARTNERSHIP, SUITE 2400, 600 CONGRESS AVENUE, AUSTIN, TX, 78701
NUMBER OF CLAIMS: 126
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Page(s)
LINE COUNT: 5666
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The use of non-viral delivery of therapeutically effective compositions through aerosol for therapy or research purpose has been limited by the

low efficiency mainly caused by an inefficient delivery system and destruction of formulation (gene and/or delivery system) by aerosol shearing power. This invention develops formulations that are established polymer combination formulations. The formulations are highly efficient in delivering genes in vivo through aerosol and are able to protect the delivered gene from the destruction by aerosol shearing power.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **153312-64-2**, Dmrie
(polymer combinations that result in stabilized aerosols for gene delivery to the lungs)
RN 153312-64-2 USPATFULL
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



L54 ANSWER 30 OF 37 USPATFULL

ACCESSION NUMBER:	2002:112289 USPATFULL
TITLE:	DNA vaccines for farm animals, in particular bovines and porcines
INVENTOR(S):	Audonnet, Jean-Christophe Francis, Lyon, FRANCE Fischer, Laurent Bernard, Sainte Foy Les Lyon, FRANCE Barzu-Le-Roux, Simona, Lentilly, FRANCE

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002058021	A1	20020516
APPLICATION INFO.:	US 2001-760574	A1	20010116 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	FR 2000-798	20000121
	US 2000-193126P	20000330 (60)

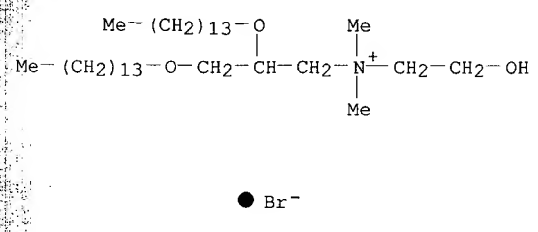
DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	William S. Frommer, Esq., c/o FROMMER LAWRENCE & HAUG LLP, 745 Fifth Avenue, New York, NY, 10151
NUMBER OF CLAIMS:	83
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	2 Drawing Page(s)
LINE COUNT:	2417

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB DNA vaccine against a pathogen affecting farm animals, in particular bovines or porcines, comprising a plasmid containing a nucleotide sequence encoding an immunogen of a pathogen of the animal species considered, under conditions allowing the in vivo expression of this sequence, and a cationic lipid containing a quaternary ammonium salt, of formula ##STR1##

in which R1 is a saturated or unsaturated linear aliphatic radical

having 12 to 18 carbon atoms, R2 is another aliphatic radical containing 2 or 3 carbon atoms, and X a hydroxyl or amine group, this lipid being preferably DMRIE.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **153312-64-2**, Dmrie
(improved DNA vaccines for livestock)
RN 153312-64-2 USPATFULL
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



L54 ANSWER 31 OF 37 USPATFULL

ACCESSION NUMBER:	2002:32536 USPATFULL
TITLE:	Compositions and methods for in vivo delivery of polynucleotide-based therapeutics
INVENTOR(S):	Manthorpe, Marston, San Diego, CA, UNITED STATES Hartikka, Jukka, San Diego, CA, UNITED STATES Sukhu, Loretta, San Diego, CA, UNITED STATES
PATENT ASSIGNEE(S):	Vical Incorporated, San Diego, CA (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002019358	A1	20020214
APPLICATION INFO.:	US 2001-839574	A1	20010423 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-198823P	20000421 (60)
	US 2000-253153P	20001128 (60)

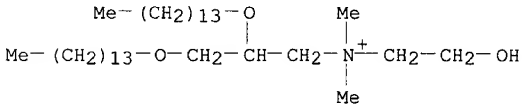
DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	STERNE, KESSLER, GOLDSTEIN & FOX PLLC, 1100 NEW YORK AVENUE, N.W., SUITE 600, WASHINGTON, DC, 20005-3934
NUMBER OF CLAIMS:	163
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	29 Drawing Page(s)
LINE COUNT:	4605

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to pharmaceutical compositions and methods to improve expression of exogenous polypeptides into vertebrate cells in vivo, utilizing delivery of polynucleotides encoding such polypeptides. More particularly, the present invention provides the use of salts, in particular sodium and potassium salts of phosphate, in aqueous solution, and auxiliary agents, in particular detergents and surfactants, in pharmaceutical compositions and methods useful for direct polynucleotide-based polypeptide delivery into the cells of vertebrates.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **153312-64-2**, Dmrie **208040-06-6**, Gap dlrie
299207-54-8, Gap-dmorie

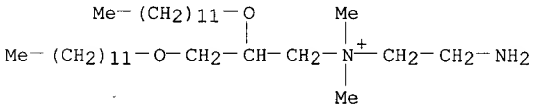
(compns. and methods for in vivo delivery of polynucleotide-based therapeutics)

RN 153312-64-2 USPATFULL
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



● Br^-

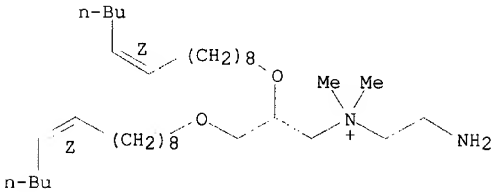
RN 208040-06-6 USPATFULL
CN 1-Propanaminium, N-(2-aminoethyl)-2,3-bis(dodecyloxy)-N,N-dimethyl-, bromide (9CI) (CA INDEX NAME)



● Br^-

RN 299207-54-8 USPATFULL
CN 1-Propanaminium, N-(2-aminoethyl)-N,N-dimethyl-2,3-bis[(9Z)-9-tetradecenyloxy]-, bromide (9CI) (CA INDEX NAME)

Double bond geometry as shown.



● Br^-

L54 ANSWER 32 OF 37 USPATFULL
ACCESSION NUMBER: 1998:115721 USPATFULL
TITLE: Dry powder formulations of polynucleotide complexes
INVENTOR(S): Szoka, Jr., Francis C., San Francisco, CA, United States
Rolland, Alain, The Woodlands, TX, United States
Wang, Jinkang, San Francisco, CA, United States

Searched by Barb O'Bryen, STIC 308-4291

PATENT ASSIGNEE(S): Regents of the University of California, Oakland, CA, United States (U.S. corporation)

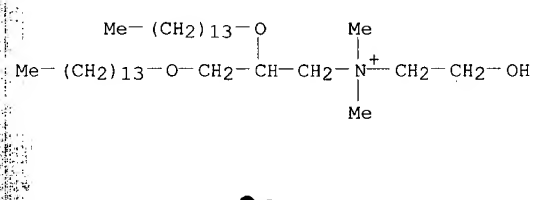
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5811406		19980922
APPLICATION INFO.:	US 4822544		19950609 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. 482110, filed on 7 Jun 1995 And Ser. No. 485430, filed on 7 Jun 1995

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Ketter, James
ASSISTANT EXAMINER: Yucel, Irem
LEGAL REPRESENTATIVE: Crosby, Heafey, Roach & May
NUMBER OF CLAIMS: 19
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 32 Drawing Figure(s); 23 Drawing Page(s)
LINE COUNT: 763
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Polynucleotide complexes are stabilized by adding a cryoprotectant compound and lyophilizing the resulting formulation. The lyophilized formulations are milled or sieved into a dry powder formulation which may be used to deliver the polynucleotide complex. Delivery of the polynucleotide to a desired cell tissue is accomplished by contacting the tissue with the powder to rehydrate it. In a preferred embodiment, a dry powder formulation is used to transfer genetic information to the cells of the respiratory tract.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **153312-64-2D**, Dmrie, polynucleotide complexes
(dry powder formulations of polynucleotide complexes for inhalation delivery to the respiratory tract)
RN 153312-64-2 USPATFULL
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)



L54 ANSWER 33 OF 37 MEDLINE
ACCESSION NUMBER: 97378926 MEDLINE
DOCUMENT NUMBER: 97378926 PubMed ID: 9234523
TITLE: Mucosal immunization with DNA-liposome complexes.
AUTHOR: Klavinskis L S; Gao L; Barnfield C; Lehner T; Parker S
CORPORATE SOURCE: Department of Immunology, Guy's Hospital Medical School, United Medical School of Guy's Hospital, London, UK.
SOURCE: VACCINE, (1997 Jun) 15 (8) 818-20.
Journal code: 8406899. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 19971105
Last Updated on STN: 19971105
Entered Medline: 19971023

ABSTRACT:
The mucosal surfaces represent the primary site for transmission of several viruses including HIV. To prevent mucosal transmission and dissemination to the regional lymph nodes, an effective HIV vaccine may need to stimulate immune responses at the genital and rectal mucosa. Optimal induction of mucosal immunity in general requires targeting antigens to the specialized antigen presenting cells of mucosal associated lymphoid tissues. The nasal mucosa may provide a simple, non-invasive route to deliver DNA encoding the introduced gene to stimulate mucosal immunity. As a first step to evaluate the feasibility of this approach, we have investigated as a model system, systemic and mucosal immune responses elicited to firefly luciferase generated by DNA immunization. Incorporating DNA into liposomes with cationic lipids enhanced luciferase expression in nasal tissue, and was associated with induction of a humoral response in serum and vaginal fluids and also a proliferative and cytotoxic T lymphocyte response in the spleen and iliac lymph nodes draining the genital and rectal mucosa.

CONTROLLED TERM: Check Tags: Animal; Female; Support, Non-U.S. Gov't
***AIDS Vaccines: AD, administration & dosage**
AIDS Vaccines: IM, immunology
Administration, Intranasal
Ammonium Compounds
DNA, Viral: IM, immunology
Enzyme-Linked Immunosorbent Assay
*HIV Antibodies: BI, biosynthesis
HIV-1: GE, genetics
*HIV-1: IM, immunology
*Immunity, Mucosal
Lipids
*Liposomes
Mice
Phosphatidylethanolamines
T-Lymphocytes: IM, immunology
T-Lymphocytes, Cytotoxic: IM, immunology
***Vaccines, DNA: AD, administration & dosage**
Vaccines, DNA: IM, immunology

Registry records for hits from Medline & Toxcenter printed at end of search

CAS REGISTRY NO.: 153312-64-2 **((3-dimyristyloxypropyl)(dimethyl)(hydroxyethyl)ammonium)**; 76391-83-8 (1,2-dielaidoylphosphatidylethanolamine)
CHEMICAL NAME: 0 (AIDS Vaccines); 0 (Ammonium Compounds); 0 (DNA, Viral); 0 (HIV Antibodies); 0 (Lipids); 0 (Liposomes); 0 (Phosphatidylethanolamines); 0 (Vaccines, DNA)

L54 ANSWER 34 OF 37 TOXCENTER COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:191641 TOXCENTER
COPYRIGHT: Copyright 2003 ACS
DOCUMENT NUMBER: CA13322308810E
TITLE: Transfected human dendritic cells to induce antitumor immunity
AUTHOR(S): Rughetti, A.; Biffoni, M.; Sabbatucci, M.; Rahimi, H.; Pellicciotta, I.; Fattorossi, A.; Pierelli, L.; Scambia, G.; Lavitrano, M.; et al.
CORPORATE SOURCE: Department of Experimental Medicine and Pathology, Universita di Roma 'La Sapienza', Rome, 00161, Italy.
SOURCE: Gene Therapy, (2000) Vol. 7, No. 17, pp. 1458-1466.
CODEN: GETHEC. ISSN: 0969-7128.
COUNTRY: ITALY

DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2000:648161
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20030225

ABSTRACT:
Dendritic cells are professional antigen-presenting cells able to prime naive T lymphocytes and regulate steadily the delicate balance between tolerance and activation during the immune response. In past years several reports have shown that genetically engineered dendritic cells (DCs) can be a powerful tool for inducing an antigen-specific immune response. The use of such modified antigen-presenting cells is a real working hypothesis in preclin. studies and in clin. **vaccination** approaches for cancer treatment. The definition of optimal transfection conditions for preserving DC survival and functionality is necessary to design a correct **immunotherapeutic** protocol. Different lipid-based transfection compds. were studied for their effects on DC survival, phenotype and functional properties. All the transfection procedures were able to select DCs with a higher expression of activation and costimulatory mols. (ie MHCII-DR, CD83, CD86, CD25) than the untreated DCs. However, only two compds. (LipofectAMINE PLUS and FuGENE 6), preserved or even increased the immunopotency of DCs as antigen-presenting cells. These protocols were applied to modify DCs to express an epithelial tumor-assocd. antigen, MUC1, and such cells were able to induce in vitro a specific immune response in healthy donors.

CLASSIFICATION CODE: 15-2
SUPPLEMENTARY TERMS: Miscellaneous Descriptors
dendritic cell transfection tumor immunity
REGISTRY NUMBER: 105488-80-0 (Clonfectin)
128835-92-7 (Lipofectin)
144189-73-1 (DOTAP)
158571-62-1 (LipofectAMINE)
189203-05-2 (DMRIE-C)
214210-13-6 (FuGENE 6)

L54 ANSWER 35 OF 37 TOXCENTER COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:65194 TOXCENTER
DOCUMENT NUMBER: 20336362 PubMed ID: 10880015
TITLE: Studies of direct intratumoral gene transfer using cationic lipid-complexed plasmid DNA
AUTHOR(S): Clark P R; Stopeck A T; Ferrari M; Parker S E; Hersh E M
CORPORATE SOURCE: Arizona Cancer Center, University of Arizona, Tucson 85724, USA
SOURCE: CANCER GENE THERAPY, (2000 Jun) 7 (6) 853-60.
Journal Code: 9432230. ISSN: 0929-1903.
COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDLINE
OTHER SOURCE: MEDLINE 2000493631
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20011116

ABSTRACT:
Cationic lipid-mediated gene transfer is a safe and effective means of delivering potent immunomodulatory cytokines directly into tumors. This approach avoids undesirable side effects, including systemic toxicities. To investigate key factors affecting intratumoral (i.t.) gene transfer, cationic lipid-DNA complexes were injected into subcutaneous human melanoma tumors in severe combined immunodeficient mice. Animals received i.t. injections of VR1103, a DNA plasmid encoding the gene for human interleukin-2 (IL-2), either alone or complexed with the cationic lipid N-(1-(2,3-dimyristyloxypropyl)-N,N-dimethyl-(2-hydroxyethyl) ammonium bromide/dioleoyl phosphatidylethanolamine (DMRIE/DOPE). Tumors were subcultured and supernatants were tested for IL-2

secretion by enzyme-linked immunosorbent assay. IL-2 secretion was consistently higher when lipid:DNA (L:D) complexes were formulated at high L:D ratios (wt/wt), and IL-2 transgene expression increased in a DNA dose-dependent manner. A comparison of naked plasmid and lipid-complexed DNA revealed that lipid complexes were more effective for i.t. gene transfer. Using an enhanced green fluorescent protein reporter plasmid and flow cytometry, i.t. transfection efficiency was 1.74% (+/- 1.08%). Tumor injection technique, including injection volume and location, had a limited impact on i.t. gene transfer. These results indicate that the formulation and dosage of cationic L:D complexes, but not injection technique, play a key role in determining the level of i.t. transgene expression.

CONTROLLED TERM: Check Tags: Animal; Human; Support, Non-U.S. Gov't
*Ammonium Compounds: ME, metabolism
*DNA: ME, metabolism
Flow Cytometry
Gene Therapy
*Glycerophospholipids: ME, metabolism
Immunotherapy
Interleukin-2: BI, biosynthesis
Interleukin-2: GE, genetics
*Lipids: ME, metabolism
Luminescent Proteins: ME, metabolism
*Melanoma: GE, genetics
Melanoma: ME, metabolism
Mice
Mice, SCID
Mice, Transgenic
*Plasmids: GE, genetics
*Skin Neoplasms: GE, genetics
Skin Neoplasms: ME, metabolism
*Transfection: MT, methods
Tumor Cells, Cultured

REGISTRY NUMBER: 147336-22-9 (green fluorescent protein)
[redacted] (3-dimyristyloxypropyl)(dimethyl)(h ydroxyethyl)ammonium)
9007-49-2 (DNA)

CHEMICAL NAME: 0 (1,2-dioleoyl-glycero-3-phosphatidyl ethanolamine); 0 (Ammonium Compounds); 0 (Glycerophospholipids); 0 (Interleukin-2); 0 (Lipids); 0 (Luminescent Proteins); 0 (Plasmids)

L54 ANSWER 36 OF 37 TOXCENTER COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:46146 TOXCENTER
DOCUMENT NUMBER: 20311213 PubMed ID: 10854152
TITLE: Intratumoral interleukin 2 for renal-cell carcinoma by direct gene transfer of a plasmid DNA/DMRIE/DOPE lipid complex
AUTHOR(S): Hoffman D M; Figlin R A
CORPORATE SOURCE: Department of Medicine, University of California, Los Angeles, School of Medicine, 90095, USA
SOURCE: WORLD JOURNAL OF UROLOGY, (2000 Apr) 18 (2) 152-6. Journal Code: 8307716. ISSN: 0724-4983.
COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
(CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDLINE
OTHER SOURCE: MEDLINE 2000311213
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20011116

ABSTRACT:

Metastatic renal-cell carcinoma (RCC) is not responsive to conventional cytotoxic chemotherapy, but a subset of patients achieve a durable remission with the use of interleukin-2 (IL-2). IL-2 is currently the only Food and Drug Administration (FDA)-approved treatment for metastatic RCC, and it benefits 10-20% of those who receive it. However, it is accompanied by significant, occasionally life-threatening toxicity. Attempts to maintain the efficacy of IL-2 while minimizing systemic side effects have led to the development of IL-2 gene therapies. Leuvectin is a plasmid DNA/lipid complex composed of a plasmid DNA expression vector (VCL-1102, 30) encoding human IL-2 complexed in a 5:1 mass ratio with DMRIE/DOPE lipid (1,2-dimyristyloxypropyl-3-dimethylhydroxyethyl ammonium bromide/dioleoylphosphatidyl ethanolamine), which has been developed for the treatment of malignancy. DMRIE/DOPE is a cationic lipid that has been shown to facilitate in vitro transfection of plasmid DNA. It has been demonstrated that in vitro transfection with the IL-2 plasmid DNA/DMRIE/DOPE complex results in the expression of sustained levels of biologically active IL-2. Established human tumor cell lines and primary human tumor cells obtained from biopsies are readily transfected in vitro, resulting in the expression of IL-2. Following in vitro transfection, IL-2 expression has been found to persist for up to several weeks in primary tumor cells. In preclinical efficacy studies in a murine model of renal-cell carcinoma the direct intratumoral administration of an IL-2 plasmid DNA/DMRIE/DOPE complex resulted in complete tumor regression in the majority of mice. In preclinical animal-safety studies, repeated administration of Leuvectin was safe and well tolerated. Following these promising preclinical trials, Leuvectin has been taken into clinical trial. The results of two early studies indicate that Leuvectin is safe, is free of systemic toxicity, and has biologic activity.

CONTROLLED TERM: Check Tags: Human; Male
Aged
Ammonium Compounds: PK, pharmacokinetics
Biopsy
*Carcinoma, Renal Cell: SC, secondary
*Carcinoma, Renal Cell: TH, therapy
*Gene Transfer Techniques
Immunotherapy
Interleukin-2: AE, adverse effects
*Interleukin-2: GE, genetics
Interleukin-2: TU, therapeutic use
Kidney Neoplasms: PA, pathology
Lipids: PK, pharmacokinetics
*Liver Neoplasms: SC, secondary
*Liver Neoplasms: TH, therapy
Lung Neoplasms: SC, secondary
Lung Neoplasms: TH, therapy
*Plasmids
Recombinant Proteins: GE, genetics
Recombinant Proteins: TU, therapeutic use
Transgenes

REGISTRY NUMBER: [redacted]((3-dimyristyloxypropyl)(dimethyl)(hydroxyethyl)ammonium)

CHEMICAL NAME: 0 (Ammonium Compounds); 0 (Interleukin-2); 0 (Lipids); 0 (Plasmids); 0 (Recombinant Proteins)

L54 ANSWER 37 OF 37 TOXCENTER COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:66643 TOXCENTER

DOCUMENT NUMBER: 99438205 PubMed ID: 10506635

TITLE: **Immunotherapy** of advanced malignancy by direct gene transfer of an interleukin-2 DNA/DMRIE/DOPE lipid complex: phase I/II experience

AUTHOR(S): Galanis E; Hersh E M; Stopeck A T; Gonzalez R; Burch P; Spier C; Akporiaye E T; Rinehart J J; Edmonson J; Sobol R E; Forscher C; Sondak V K; Lewis B D; Unger E C; O'Driscoll M; Selk L; Rubin J

CORPORATE SOURCE: Mayo Clinic and Mayo Foundation, Rochester, MN 55905, USA.

galanis.evanthia@mayo.edu
SOURCE: JOURNAL OF CLINICAL ONCOLOGY, (1999 Oct) 17 (10) 3313-23.
Journal Code: 8309333. ISSN: 0732-183X.
COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
(CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDLINE
OTHER SOURCE: MEDLINE 1999438205
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20011116

ABSTRACT:
PURPOSE: We have completed a phase I study, followed by three phase I/II studies, in patients with metastatic melanoma, renal cell carcinoma (RCC), and sarcoma in order to evaluate the safety, toxicity, and antitumor activity of Leuvectin (Vical Inc, San Diego, CA), a gene transfer product containing a plasmid encoding human interleukin (IL)-2 formulated with the cationic lipid 1, 2-dimyristyloxypropyl-3-dimethyl-hydroxyethyl ammonium bromide/dioleyl-phosphatidyl-ethanolamine (DMRIE/DOPE) and administered intratumorally. PATIENTS AND METHODS: Twenty-four patients were treated in the phase I study. Leuvectin doses were 10 microg, 30 microg, or 300 microg weekly for 6 weeks. In three subsequent phase I/II studies, a total of 52 patients (18 with melanoma, 17 with RCC, and 17 with sarcoma) were treated with further escalating doses of Leuvectin: 300 microg twice a week for 3 weeks, 750 microg weekly for 6 weeks, and 1,500 microg weekly for 6 weeks. RESULTS: There were no drug-related grade 4 toxicities and only one grade 3 toxicity, but the majority of patients experienced mild constitutional symptoms after treatment. In the phase I/II studies, 45 patients were assessable for response (14 with RCC, 16 with melanoma, and 15 with sarcoma). Two patients with RCC and one with melanoma have achieved partial responses lasting from 16 to 19 months and continuing. In addition, two RCC, three melanoma, and six sarcoma patients had stable disease lasting from 3 to 18 months and continuing. The plasmid was detected by polymerase chain reaction assay in the posttreatment samples of 29 of 46 evaluated patients. Immunohistochemistry studies on serial biopsy specimens showed increased IL-2 expression and CD8(+) infiltration after treatment in the tumor samples of several patients (12 and 16, respectively). CONCLUSION: Direct intratumoral injection of Leuvectin is a safe and possibly effective **immunotherapeutic** approach in the treatment of certain tumor types.

CONTROLLED TERM: Check Tags: Female; Human; Male
Adult
Aged
Ammonium Compounds: TU, therapeutic use
Antigens, CD8: AN, analysis
Carcinoma, Renal Cell: PA, pathology
*Carcinoma, Renal Cell: TH, therapy
Dose-Response Relationship, Drug
*Gene Therapy
*Gene Transfer Techniques
Immunohistochemistry
Interleukin-2: GE, genetics
Interleukin-2: PK, pharmacokinetics
*Interleukin-2: TU, therapeutic use
Kidney Neoplasms: PA, pathology
*Kidney Neoplasms: TH, therapy
Lipids: GE, genetics
Lipids: TU, therapeutic use
Melanoma: PA, pathology
*Melanoma: TH, therapy
Middle Age
Plasmids: GE, genetics

Polymerase Chain Reaction
Sarcoma: PA, pathology
*Sarcoma: TH, therapy
Skin Neoplasms: PA, pathology
*Skin Neoplasms: TH, therapy

REGISTRY NUMBER: 153812-64-2, ((3-dimyristyloxypropyl)(dimethyl)(hydroxyethyl)ammonium)

CHEMICAL NAME: 0 (Ammonium Compounds); 0 (Antigens, CD8); 0 (Interleukin-2); 0 (Lipids); 0 (Plasmids)

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FILE 'REGISTRY' ENTERED AT 15:22:35 ON 27 FEB 2003
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DICTIONARY FILE UPDATES:  26 FEB 2003  HIGHEST RN 495373-62-1

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Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> s  153312-64-2 or  189203-05-2

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               (153312-64-2/RN)
             1 189203-05-2
               (189203-05-2/RN)
L55          2 153312-64-2 OR  189203-05-2

=> d ide 1-2; fil hom

L55  ANSWER 1 OF 2  REGISTRY  COPYRIGHT 2003 ACS
RN   189203-05-2  REGISTRY
CN   Cholest-5-en-3-ol (3.beta.)-, mixt. with N-(2-hydroxyethyl)-N,N-dimethyl-
     2,3-bis(tetradecyloxy)-1-propanaminium bromide (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-,
     bromide, mixt. contg. (9CI)
OTHER NAMES:
CN   Cholesterol mixt. with DMRIE
CN   DMRIE-C
CN   DMRIE-cholesterol mixt.
FS   STEREOSEARCH
MF   C35 H74 N O3 . C27 H46 O . Br
CI   MXS
SR   CA
LC   STN Files:   BIOSIS, CA, CAPLUS, TOXCENTER, USPATFULL

     CM   1

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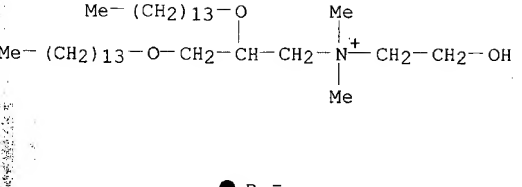
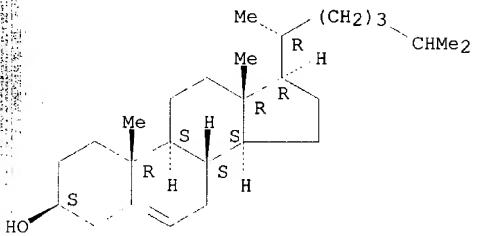


CM 2

CRN 57-88-5
CMF C27 H46 O

Absolute stereochemistry.



32 REFERENCES IN FILE CA (1962 TO DATE)
32 REFERENCES IN FILE CAPLUS (1962 TO DATE)

L55 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2003 ACS
RN [redacted] REGISTRY
CN 1-Propanaminium, N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-, bromide (9CI) (CA INDEX NAME)
OTHER NAMES:
CN DMRIE
CN N-[1-(2,3-Ditetradecyloxy)propyl]-N,N-dimethyl-N-hydroxyethylammonium bromide
DR 146659-77-0
MF C35 H74 N O3 . Br
CI COM
SR CA
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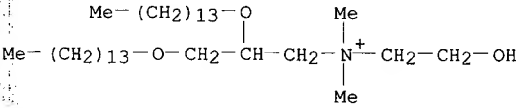
CRN (191980-81-1)



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